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THE PSYCHIATRIST, HIS OBLIGATIONS AND OPPORTUNITIES

CHAIRMAN'S ADDRESS

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It is a difficult task to write this type of essay, particularly for one whose observations and comments come largely out of an experience that has been for the most part with patients and with teaching, an experience that does not necessarily lend itself to the development of efficiency in philosophical commentary. Charburough, 2,000 years ago said, "It does not take a great mind to make simple things complicated, but a very great mind to make complicated things simple." I hope my discussion will not complicate things too much. These remarks will possibly be more an inventory of things I should have done and would yet like to do.

I suppose this choice of topic stems from a principle of psychotherapy that my old chief, Adolf Meyer, often presented to patients: the reminder that life is replete with opportunities for satisfaction that must be endlessly sought for. The implications of this reminder of the perfectly obvious has given to me a special meaning for the word "opportunity." Any profession gives endless opportunity for service, but psychiatry is a field that involves more of the person or the soul; is more intimate in its relationships and involves more time, more struggle to be wise, tolerant, flexible, understanding, and patient; the capacity to hear the startling and not be startled; the capacity to be hurt and not show it or to be angry or annoyed and be able to react in a way that will be constructive to the patient. These are some of the reasons why I think the psychiatrist should search, with profit to himself, to his patients, and to society as a whole, for the opportunities that are constantly unfolding. There is so much to be done that the psychiatrist now has to choose the type of psychiatry he is fitted for and able to do.

EXPANSION OF THE FIELD OF PSYCHIATRY

The present-day psychiatrist finds himself attempting to fill quite a different role than that of his counterpart 25 years ago. He has come out of his more or less protected environment of the institution and entered into the treatment of the individual patient. Someone pointed out recently that the public health officer and the psychiatrist have now traded places. The doctor of public health, who is interested in the health of the masses, is increasing his field to include the mental health of the masses; the doctors of the mind, who formerly were interested largely in treating the mental problems of great numbers of persons, are now turning to the treatment of individuals. The psychiatrist is no longer the sole keeper of the keys; there are others, such as the clinical psychologist, the psychiatric social worker, the psychiatric nurse, personnel counsellors, the minister, and the lay psychotherapist. The psychiatrist cannot ignore these persons, all of whom are capable of making some considerable contribution to the field of psychological medicine. We must know something about their methods, how they work, and why they are able to help. We must learn how we may pool our knowledge for the greater good of the patient and how to reach a larger number of patients. Attempts at cooperation are being made by the American Psychiatric Association in its joint committees with the American Psychological Association, its committees on psychiatric social work, and through joint teaching programs in schools of religion, law, and similar cooperative activities. There can be no doubt that the general recognition of the vastness of the problem of mental illness, the increasing knowledge of the social factors in its causation, the emphasis on the early years of life as a particularly important period in the dynamics of mental illness, the greater understanding by the medical profession of emotional factors in disease brought to focus by the war have all made it possible and necessary for these new professions to enter the field of psychiatry.

It is time for the psychiatrist to look at the present status of this field that was once only our own and no longer is, and define for himself the kind of job he is best fitted for. We have been talking a long time about industry and the importance of placing persons in situations

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for which they show special aptitudes. Psychiatry now is in much the same position as a very large industry. Gregory Zilboorg stated recently [1] that "psychiatry seems to claim a major role in medical education, in public life, juvenile delinquency, criminology, penology, sociology and even international and military problems." He states further that the psychiatrist in order to be able to fill this role "must acquire some knowledge of anthropology, sociology and history, the emotional as well as intellectual aspects of morality, ethics, religion and philosophy." Most of this he believes the psychiatrist must find for himself, because it is not provided in his graduate or postgraduate training. This mushrooming growth of psychiatry is confusing both to the postgraduate student and to the psychiatrist who has been practicing for a long time. Dr. Leo Bartemeier in his presidential address before the American Psychiatric Association recently called attention to some of the dangers involved in the rapid and possibly too rapid taking over of psychiatry by the psychoanalytic school of psychotherapy. He pointed out that the nonanalytically trained psychiatrist in his efforts to keep up with the times might become more interested in mechanisms involved than in the patient. He was reassuring in his reminder that psychoanalysis is a special type of therapy useful in many of the problems of psychiatry but that by no means are physicians in this field interested in taking over all the tasks that have been done by psychiatrists in the past. Dr. Bartemeier's remarks should be enlightening to the psychiatric resident who might wish to confine his activities to therapy alone.

PSYCHIATRY AND THE GENERAL PRACTITIONER

Any review of the opportunities and obligations facing the practicing psychiatrist today should include an inquiry into psychiatry's relationships with its colleagues in medicine, what they think of psychiatry, what they demand of it, how much isolation psychiatrists practice in these contacts, and how the rapport can be improved. In discussion of this topic, I would like to describe a program of postgraduate teaching in psychiatry given to general practitioners a few months ago in Tennessee. This program was sponsored by the Commonwealth Fund, the University of Tennessee School of Medicine, Vanderbilt School of Medicine, and the Tennessee State Medical Society. For a period of two years, 46 population centers were visited by an instructor once a week for 10 weeks. The course consisted of lectures, clinical demonstrations, and a few movies on psychiatric subjects. Local physicians were encouraged to ask for consultations on their own patients. A questionnaire follow-up gave the instructors an opportunity to find out what this group thought of the program.

Most of them felt that the course was inadequate. Many had criticisms of the speaker. They disliked his manner of presentation, said that he was too didactic, that he was "a nice fellow who knew his field" but was unable to present it in a way that would be of practical benefit to the practitioner, that he was too theoretical, that he used too many psychoanalytic terms, did not present enough patients, was too young in his field to give the physician confidence in him, and that his consultations were not very helpful to the physician in his treatment of the problem.

This experiment gave me the impression that we have much to learn about short-term presentation of material to the physician who has had little training in psychiatry. The Minnesota Pilot Plan (1946), in which a small team of psychiatrists gave a two week course in psychotherapy to a group of 25 physicians brought in for this period of intensive study, is a type of program that seems to have promise. A report [2] at the last meeting of the American Psychiatric Association of a survey of the influence of one short course in psychiatry given to a group of Navy physicians in the Philadelphia area revealed that a large number of men were stimulated to become specialists in psychiatry and that among those who did not later specialize there was the feeling that the course had benefited them markedly in their chosen field of practice.

The Tennessee program pointed up the following facts.

1. The physician is interested in finding out what psychiatrists are like and what they have to offer him. This was shown by the fact that a significant number of physicians (975) signed up for the course, and the meetings were well attended. 2. The physician would like to have as a teacher a person who is enthusiastic, who "talks his language," who does not repel him by the use of too many sex terms or too much emphasis on sex mechanisms, who can take the mystery out of mental illness and put it in a category that is not too far removed from the types of problems that he sees every day. 3. He has many problems that he recognizes as psychiatric and he wants to know how to manage them in a better way. Out of this real need came the many requests for more practical suggestions.

In my opinion this program has brought to light both stimulating opportunities for work and revelation of some of the deficiencies of many psychiatrists, for psychiatrists do have a definite responsibility with respect to their colleagues in medicine and other specialties, and they must be aware of this in their management of the patients referred to them. The different attitudes of the referring physician must be considered. Some physicians refer patients to the psychiatrist with the expectation that they as the family doctors will participate in the treatment. They should participate in many instances. The psychiatrist should consider whether the physician knows how to work with him, whether he is able to work with the physician, and whether there is an opportunity for for teaching. The psychiatrist should have his thoughts about the patient well enough organized to give the referring physician some help in understanding the patient and possibly to give a background that will promote better collaboration in other cases. There are many problems involved in just this issue of collaboration.

Knowledge of the physician and his background is essential for any program of mutual participation in treatment. There are physicians who are not interested in psychiatric patients and who, when they refer a patient, expect the psychiatrist to treat him. It is sometimes difficult for the psychiatrist to explain that his schedule will

1. Zilboorg, G.: Psychiatric Perspectives of Today, Bull. New York Acad. Med. **25**: 577 (Sept.) 1949.

2. Caveny, E. L., and Strecker, E. A.: Subsequent Nation-Wide Effects of World War II, Navy Psychiatric Training Program, read before the American Psychiatric Association, Atlantic City, N. J., May 12-16, 1952.

not permit an addition for several months. It is often embarrassing to turn down a consultation or refuse to accept an emergency case because of the pressure of appointments and regular teaching responsibilities. I have often heard the statement "I don't ever send any patients to you because it is always two or three weeks before you can see one, and the patient may be dead by then." The answer to this and other questions I have raised is a long-range one suggested by the references made above to different types of educational programs. The beginning must be made in the medical school, when the student should become as familiar with the emotional causes of illness and the interrelationships suggested by the term psychosomatic (Plant has suggested that the term sociopsychosomatic replace this term) as he is with the causes of heart disease. The next step might be provided by the psychiatrist who will associate himself with other physicians in medical meetings, general staff rounds, in rounds on the various specialty departments such as gynecology and obstetrics, surgery, medicine, pediatrics, and ear, nose, and throat. He should learn to express himself simply and interestingly before medical groups when the opportunity occurs. A few years ago Dr. William Menninger talked before our local academy of medicine on the general formulations and meanings of psychiatry. He did it without one mention of the ego, the id, or other special psychiatric entities. The response was enthusiastic and laudatory, with many expressions of surprise that an address on psychiatry could be so interesting and understandable. I have felt guilty about the paucity of articles on psychiatry in our state medical journal, because the editor would publish them if they were available. I am sure that there have been requests of us for such publications from the editor.

Further efforts at the education of the physician in outlying areas must come from such programs as the short concentrated postgraduate courses (possibly subsidized by some organization), the short course by a qualified instructor that carries the material to the physician, or an arrangement in which instructors from a department of psychiatry can at frequent intervals present case material and patients before medical societies in counties that radiate from a medical center. This would facilitate more contact with physicians in these areas, who would undoubtedly refer patients to the university center.

The psychiatrist also has the obligation of cooperating with the various divisions and departments of public health. It is recognized that the preservation of good mental health is an area that should interest every psychiatrist and every public health official. A symposium held a few years ago at the American Psychiatric Association brought out the feeling that each discipline needed the other in a program of prevention, but Dr. Alan Gregg [3] pointed out that neither group knew much about the other and that until this bridge was completed their mutual needs could not be determined. Dr. Hugh Leavell [4] states that "Public health people would like to have a clearer picture of just what psychiatrists believe is involved in a community health program and what places there are in such a program for the psychiatrists themselves." He also asks for help in public health effort to weld the social and natural sciences into "a more effective tool for improving human well being." I believe that here is needed the special talent of psychiatrists with capacity for sensing the common needs of persons who live together in family units, with the capacity for the expression to groups of the facts of growth and development in simple understandable language. There are psychiatrists who are willing to learn the techniques and principles of epidemiology and mental health education that persons in the field of public health know so well, who will work with them, and who will honestly try to hink in their terms toward the end of formulation of principles for prevention of mental illness that will approach the concreteness of public health principles in other kinds of illness.

In 1933 I helped organize and participated in a mental health study [5] in Williamson County, Tennessee, a small rural county with an unusually active department of public health. This study lasted seven years and showed convincingly the potentialities for effective preventive mental health work when public health and psychiatric personnel study together the causes and methods of modification of family and community situations that seem to promote the spread of mental illness.

SUMMARY AND CONCLUSIONS

The psychiatrist today should have a sense of the opportunity for satisfaction afforded by his profession. He should appreciate the breadth of his field but not spread his efforts too thin nor be frightened by the forces of change. He should be aware of his community problems, should participate in its programs for health, and should learn to organize his ideas and express them simply. The psychiatrist should be able to work with his colleagues in other fields of medicine toward the general end of mutual respect and better collaborative effort. Teaching, research, and writing should be looked upon as essential in psychiatry as in any other scientific discipline. Finally, the psychiatrist should never forget the patient.

3. Gregg, A.: Psychiatry in Public Health, Am. J. Psychiat. **107**: 330 (Nov.) 1950.

4. Leavell, H. R.: What Public Health Needs from Psychiatry, Am. J. Psychiat. **107**: 321 (Nov.) 1950.

5. Roth, W. F., Jr.; Williams, W. C., and Luton, F. H.: Relationship of Mental Hygiene to Local Health Department Program, Am. J. Pub. Health **32**: 1005 (Sept.) 1942.

X-Ray Exposures.—Some observers have been reporting the occurrence of fractures of the femoral neck in a small percentage of their patients who have received heavy irradiation for neoplasm, usually of the uterus. Some of these fractures occurred less than a year after treatment, others not until almost four years had elapsed, but in all of them it seemed clear that the lesion was caused by intense irradiation of the bone rather than by trauma or by spread of the neoplasm. . . . Bear in mind that ionization is injurious to living tissue. . . . The best policy is to employ radiation only when less dangerous agents are clearly inferior. In therapy this means employing it only for those cases of neoplasm in which surgery offers less in terms of function or survival. . . . In diagnosis it means first the avoidance of repeated examinations unless the need for them is real, and second the avoidance of x-ray examinations altogether in regions and organs where the palpating finger or the endoscope will do an even better job.—P. C. Hodges, M.D., The Cumulative Effects of X-Ray Exposures, *Postgraduate Medicine*, August, 1952.

RELATIONSHIP OF SURGERY OF THE NOSE AND THROAT TO POLIOMYELITIS

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Nose and throat surgery has been accused by some as increasing the incidence and severity of poliomyelitis. Since 1938 many articles have been written refuting or substantiating this contention. A review [1] of some 28 of these references appeared last year, in which opinions were about evenly divided that the over-all incidence of poliomyelitis is increased by tonsillectomy and adenoidectomy, either recent or ancient; however, a preponderance of opinions held that if poliomyelitis has been contracted following a recent tonsillectomy and adenoidectomy there is an increased likelihood that the bulbar type of the disease will occur. Through the cooperation of the Los Angeles county and city health departments and the Communicable Disease Service of the Los Angeles County Hospital, it has been possible to conduct a continuing three year statistical study of complete data in all cases of poliomyelitis occurring in the entire Los Angeles County during the years 1949, 1950, and 1951. This area with its 4 million population has the nation's greatest consistently high yearly incidence of this disease. These figures will be presented so that one may decide whether nose and throat surgery has caused an increase in the incidence or severity of poliomyelitis in Los Angeles County during these three years.

In the entire county there was a total of 3,601 cases of poliomyelitis in 1949 to 1951. Nose and throat surgery, other than tonsillectomy and adenoidectomy, can easily be disposed of, as records of only one polypectomy, one biopsy of the neck, and one excision of an external nasal cyst were found in this three year period. (It is interesting that each year there were more recent tooth extractions than tonsillectomies and adenoidectomies.)

INCIDENCE

The effect of recent tonsillectomy was studied first. Of 1,229 cases in 1949 [2] there were only 5 patients who underwent surgery during the 30 day period preceding the onset of the poliomyelitis. In 1950 there were 8 patients who had recently undergone tonsillectomy out of 984 cases; and in 1951 there were 7 patients out of that year's total of 1,388. Not only is this total of only 20 cases out of 3,601, or 0.55%, seemingly quite insignificant, but it is now noted that in these three years studied there were fewer cases of recently operated patients in 1951, the year of the greatest poliomyelitis incidence, than there were in the year of the least incidence, 1950. If recent surgery was a factor, the number of such cases in 1951 should have been one-third greater than those of 1950. Still further, when the month of onset of these 20 cases is considered, it is noted that fewer cases (9) occurred during the months of highest poliomyelitis incidence, July through October, than the 11 cases that occurred during the remaining months of low incidence. Therefore, so far, recent nose and throat surgery does not seem to have increased the incidence of poliomyelitis.

In order to further ascertain the effect of tonsillectomy and adenoidectomy on poliomyelitis it was next decided to determine the expected and the actual incidence of poliomyelitis in the child population of Los Angeles City of the age group 2 to 8 years inclusive, in other words, the years in which almost all tonsillectomies and adenoidectomies are performed. As in 1949,[2] reasonably accurate information on this age group of the population of Los Angeles City could be obtained. The Board of Education and the Bureau of Vital Statistics furnished population figures, and questionnaires of large hospitals in the city provided the operation figures. In

TABLE 1.—*Number of Cases of Poliomyelitis in Tonsillectomy and Adenoidectomy Age Group in Los Angeles City, by Month*

Month	1949	1950	1951	Total	Three Year Total Recent Tonsillectomies and Adenoidectomies
Jan.	18	6	26	50	0
Feb.	4	2	10	16	1
March	7	8	2	17	0
April	3	13	14	30	1
May	14	13	8	35	1
June	26	24	28	78	6
July	70	52	91	213	3
Aug.	75	66	131	272	4
Sept.	97	61	126	284	2
Oct.	62	48	97	207	0
Nov.	45	64	54	163	2
Dec.	21	36	28	85	0

1949 there were 239,369 children in this tonsillectomy and adenoidectomy age group. In this same age group there were 177 cases of poliomyelitis during the year, or 1 case per 1,352 of the tonsillectomy and adenoidectomy age population. In 1950 this population was 257,660, and there were 202 cases of poliomyelitis that year, or 1 case per 1,275. In 1951 this population had grown to 264,914 and the total number of cases for this age group was 265, or 1 case per 999.

The estimated number of tonsillectomies and adenoidectomies performed on the 2 to 8 year age group was at least the following: for 1949, 14,812; for 1950, 14,586; and for 1951, 14,544. Applying the above ratios, the expected number of cases of poliomyelitis in patients who had a tonsillectomy and adenoidectomy in 1949 is 10.9. In 1950 the expected incidence would be 11.5 cases, and in 1951, 14.5 cases. The actual number of cases of poliomyelitis that occurred in this age group in those patients who had a tonsillectomy and adenoidectomy during that year was in 1949, 10; in 1950, 8; and in 1951, 10. The difference between these estimated and actual numbers of cases of poliomyelitis that occurred in the group of patients in the age group of 2 to 8 years who had a tonsillectomy and adenoidectomy performed during that same year was of no

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Read before the Joint Meeting of the Section on Laryngology, Otology and Rhinology and the Section on Pediatrics at the 101st Annual Session of the American Medical Association, June 1, 1952.

1. Mills, C. K.: The Tonsillectomy-Poliomyelitis Problem: A Review of the Literature, Laryngoscope **61**: 1188-1196 (Dec.) 1951.

2. Miller, A. H.: Tonsillectomy and Adenoidectomy and Poliomyelitis, A. M. A. Arch. Otolaryng. **53**: 160-169 (Feb.) 1951.

significance, and again it would seem that the tonsillectomies and adenoidectomies done during those three years had no effect on the incidence of poliomyelitis during those years.

Inasmuch as the highest incidence of poliomyelitis occurs during the summer months and because the pres-

TABLE 2.—*Statistical Significance of Variation Between Expected and Actual Number of Cases of Poliomyelitis Among Patients Who Had Tonsillectomy and Adenoidectomy*

Period	Expected			Actual			Chi Square		
	1949	1950	1951	1949	1950	1951	1949	1950	1951
Entire year	10.9	11.5	14.5	10	8	10	0.07	1.07	1.39
Feb. to Nov.	9.3	9.2	11.8	10	8	10	0.05	0.16	0.27
April to Nov.	6.8	7.1	8.5	10	8	9	1.52	0.11	0.03
May to Oct.	4.3	5	5.8	8	6	9	3.18	0.20	1.76
July to Oct.	1.7	2.5	2.0	7	4	8	19.11	0.90	18.00
July to Oct. (within 30 days of onset)	1.7	2.5	2.0	1.5	2	2	0.02	0.10	0.00
				S-0.01 * = 6.63					

* S-0.01 is the significant point at 1% level of confidence.

ently discussed controversy has resulted in the fewest number of patients being operated on during these same months, the same study of expected and actual cases of poliomyelitis occurring in patients in the tonsillectomy and adenoidectomy age population was made on the basis of the 10 month, 8 month, 6 month, and 4 month periods of highest poliomyelitis incidence.

Table 1 shows the cases of poliomyelitis in Los Angeles City by the month. Again it is noted that the three year totals revealed that fewer cases followed recent tonsillectomy and adenoidectomy during the four months of highest poliomyelitis incidence, July through October, than during the remainder of the year. June had the highest total (6) of any one month. Yet, these tonsillectomies and adenoidectomies must have been done during May with its low incidence, a three year total of 35. All these findings do not seem consistent with the theory that the increased presence of the virus in the nasopharynx at the time of operation leads to an increased incidence of the disease.

TABLE 3.—*Time of Tonsillectomy and Adenoidectomy in Poliomyelitis Patients* *

No. of Years Since Surgery Was Performed	No. of Persons
1	26
2	16
3	11
4	11
5	13
6 to 10	55
11 to 15	22
16 to 20	21
21 to 25	16
26 to 30	7
Over 30	8
	206 (30%)
Never had a tonsillectomy	469 (70%)
Total	675

* Los Angeles County, exclusive of the city of Los Angeles, 1951.

In table 2 it will be noted that there was no significant statistical variation between the expected and actual cases until the four month period of July through October, 1949 and 1951, but not of 1950, was considered; however, these figures of seven cases for 1949, four cases in 1950, and eight cases in 1951 are not just patients who recently had tonsillectomies but represent those who had a tonsillectomy and adenoidectomy at any time during that year. With only those who underwent tonsillectomy and adenoidectomy 30 or less days preceding the onset of their disease considered, the last line on the chart reveals that there was no significant deviation between expected and actual cases even in the months of highest poliomyelitis incidence and lowest rate of surgery.

In 1951 an additional study could be done on the 675 cases of poliomyelitis occurring in Los Angeles County exclusive of Los Angeles City (table 3).

In the follow-up of all these patients the question was asked, "When did you ever have a tonsillectomy and adenoidectomy?" Of these patients only 206, or 30%, had had a tonsillectomy and adenoidectomy at any time in their life. At first these figures might be considered to show that the person without a tonsillectomy has more than twice as great a chance of contracting poliomyelitis as has the patient who has had a tonsillectomy. Instead,

TABLE 4.—*Percentages of Bulbar Type of Poliomyelitis in Los Angeles County*

	In All Patients	In Patients Who Recently Had a Tonsillectomy
1949	18.5	40
1950	15.0	75
1951	15.5	28.5

TABLE 5.—*Severity of Poliomyelitis in Los Angeles County*

	All Patients, %	Patients Who Recently Underwent Tonsillectomies, %
In Respirator		
1949	11.6	20.0
1950	12.0	12.5
1951	15.4	28.5
Patients Who Had Tracheotomies		
1949	9.0	20.0
1950	10.1	25.0
1951	8.1	28.5
Deaths		
1949	2.1	20.0
1950	1.7	12.5
1951	1.9	14.3

numerous writers have contended that only about one-third of the general young population has had a tonsillectomy. Therefore, it should be expected that some 33% of those contracting poliomyelitis have had their tonsils and adenoids removed. There is no significant variation between the figures of 33% and 30%.

TYPE OF DISEASE

In Los Angeles County the percentage of patients with the bulbar type poliomyelitis has been fairly constant.

Table 4 shows that the bulbar type of poliomyelitis seemed to develop in a larger percentage of the patients who recently had tonsillectomies. In 1949 and in 1951 this percentage was twice as great, and in 1950 it was five times as great. The number of patients who recently underwent tonsillectomies was so small, only 20, that a statistical study and comparison of expected and actual bulbar cases would have little value statistically; however, if future years' surveys consistently reveal the same ratio it would have to be conceded that the bulbar type of poliomyelitis does seem to develop about twice as often in patients who had tonsillectomies 30 days or less before the onset of their disease.

SEVERITY

Table 5 compares the severity of poliomyelitis in all patients and those who recently had tonsillectomies. In two years out of three the percentage of patients requiring a respirator was twice as great in those who recently had tonsillectomies. In all three years two and one-half times as great a percentage needed a tracheotomy. In all three years a much higher percentage of deaths occurred in patients who recently had tonsillectomies than in the entire number of patients with poliomyelitis.

TABLE 6.—*Comparison of Type and Severity of Disease in Persons Who Had and Those Who Had Not Undergone Tonsillectomy at Any Time in Their Lives*

	No Tonsillectomy, 469	Tonsillectomy, 206
Bulbar	61	58
Tracheotomy performed	21	28
In respirator	37	41
Deaths	8	6

Table 6 compares the type and severity of the disease in the two groups of patients, those who had and those who had not had a tonsillectomy previously. Although the group with tonsillectomy was less than half as large as the group of those who had never had a tonsillectomy, the former showed almost as many cases of the bulbar type and needed as many tracheotomies and respirators as the latter group.

SUMMARY

A statistical survey was made of all the cases of poliomyelitis occurring in all of Los Angeles County during the three years 1949, 1950, and 1951, in an attempt to determine the effect of nose and throat surgery on the incidence of poliomyelitis. Tonsillectomies and adenoidectomies were the only operations noted with any degree of frequency. Yet, in the total of 3,601 cases of poliomyelitis that occurred in this three year period there were only 20 patients (½ of 1%) who had a recent tonsillectomy and adenoidectomy. The actual incidence of this disease occurring in patients who had a tonsillectomy and adenoidectomy during these three years was compared with the expected incidence in this same age group, and this statistical analysis revealed that there was no significant difference, even during the summer months of highest poliomyelitis incidence. The same finding was noted even with patients who had recently undergone tonsillectomies in the epidemic months of July through October.

A separate survey revealed that only 30% of 675 poliomyelitis patients studied had had a tonsillectomy or adenoidectomy at any time in their life. Inasmuch as one out of every three of the general young population nowadays has had a tonsillectomy and adenoidectomy, this figure is no more or less than could be expected. The bulbar type of poliomyelitis consistently developed at least twice as often in the patients who had recently had a tonsillectomy as developed in the entire yearly number of patients. So far, tracheotomy and a respirator were required on twice as many of these patients as in the patients who had not undergone tonsillectomy.

CONCLUSIONS

This continuous three year study seems to reveal that in Los Angeles County in 1949, 1950, and in 1951 nose and throat surgery did not increase the incidence of poliomyelitis significantly at any time, but if a tonsillectomy and adenoidectomy had been performed in less than 30 days before the onset of the disease the likelihood of the bulbar type of the disease developing in these patients and of their being more severely ill was twice as great as in the rest of the poliomyelitis patients.

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OCCURRENCE OF POLIOMYELITIS IN RELATION TO TONSILLECTOMIES AT VARIOUS INTERVALS

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Poliomyelitis is a highly infectious disease, and most persons have had it in a subclinical form by the time they become adults.[1] Recognizable or paralytic cases are relatively few, and the ratio of subclinical to clinical infections is estimated at upwards of 100 to 1. Little that we know concerning the disease affords a satisfactory answer to this phenomenon. Lacking a satisfactory explanation with respect to parasite factors, some have sought an explanation in predisposing causes, and for the last three decades or more emphasis has been placed on what Aycock [2] called autarceologic factors, by which is meant those physiological influences that condition a person to infection with the virus. Evidence has slowly been accumulating to show that factors other than exposure to the virus are operative. Thus, the effect of stress or trauma,[3] physical activity,[4] body type,[5] endocrine changes,[6] dietary deficiencies,[7] pregnancy,[8] tonsillectomy (early clinical studies,[9] later clinical studies,[10] and experimental work [11]), prophylactic inoculations,[12] and preceding illness [13] have been considered. All of these factors may be said to act as trigger mechanisms to cause recognizable or paralytic cases, where ordinarily the infections might have remained subclinical in nature. Recently, attention has been redirected by Armstrong to environmental features, such as seasonal variation in incidence [14] and atmospheric conditions.[15]

Studies on the relationship between tonsillectomy and poliomyelitis have been concerned principally with the occurrence of the disease within a month of the surgical

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Because of space limitations the references have been omitted from THE JOURNAL and will appear in the author's reprints.

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procedure,[16] although Aycock [9c] furnishes a large composite group in which tonsillectomy had been performed at some time prior to one month before the onset of poliomyelitis. Recently, additional reports have been made.[10] Many investigators feel that poliomyelitis occurs more frequently following recent tonsillectomy than normally would be expected and when it develops is likely to result in a more severe clinical type (bulbar or spinobulbar)[17] if tonsillectomy has preceded an attack of the disease within 30 days.

The Detroit study,[3a] in 1939, which utilized controls,* did not substantiate the finding of enhanced risk of tonsillectomy during a period of one month prior to an attack of the disease, but it did demonstrate the likelihood of a more severe type of the disease developing. The study consisted of 521 patients (including 23 who died) and 497 controls. The proportion of persons who had undergone tonsillectomies within one month preceding onset was as follows: those dead, 5.0%; patients (including those dead), 5.1%; and controls, 7.5%. Thus, in this study a higher incidence of poliomyelitis following recent tonsillectomy was not confirmed. The virus agent must be present for the disease to occur, but patients and controls were presumably and most likely exposed to the same extent when operative among intimate playmates. An analysis was made of persons who developed poliomyelitis following removal of tonsils at intervals of months and years before an attack. Tonsillectomy had been performed at some time before the occurrence of poliomyelitis in 41.3% of the 521 patients (including those who died) and 26.7% of the 497 controls. The difference would appear to be significant, considering that patients and controls came from the same environment. Among the 23 patients who died, 20, or 87%, had had a tonsillectomy at one time or another before the attack. Further, among patients with no history of tonsillectomy, the incidence of bulbar paralysis was 4.2%, while in patients who had previously undergone tonsillectomy at any time in life prior to an attack bulbar paralysis developed in 27% of instances.

These findings, which appeared to confirm Aycock's composite report, prompted the undertaking of a study to determine the tonsillectomy status of patients admitted to the Herman Kiefer Hospital, where information derived from a case history could be checked by examination of the patient. The study covers a period of 10 years, 1940 through 1949, and is the subject of this paper. The material here presented covers the more general aspects of the problem, for a breakdown of information into minutiae must await subsequent reports. The data on which this study is based cover dismissals from the Herman Kiefer Hospital during the period 1940 through 1949 and does not include the 1939 experience. The area from which patients are drawn includes the city of Detroit, Wayne County, and adjoining Macomb County. For the past two decades upwards of 85% of poliomyelitis patients from this area have been hospitalized at the Herman Kiefer Hospital. The pediatric services of two other hospitals in the area cared for the bulk of the other cases, relatively few patients being treated at home. The proportion of patients treated at the Herman Keifer Hospital is, therefore, adequate for a study of this type, except that the number and proportion of children aged through 12 years will be lower than the area experienced because the other two hospitals draw on this select age group.

TABLE 1.—*Cases, Deaths, and Fatality Rates by Clinical Type and Year*

	Total			Nonparalytic			Spinal		
Year	Cases	Deaths	Fatality Rate	Cases	Deaths	Fatality Rate	Cases	Deaths	Fatality Rate
1940	50	4	8.0	23	..	...	22	..	...
1941	95	12	12.6	33	..	...	35	2	5.7
1942	38	4	10.5	6	..	...	17	..	...
1943	35	2	5.7	2	..	...	27	..	...
1944	355	18	5.7	129	..	...	127	..	...
1945	28	3	10.7	16	..	...	4	..	...
1946	295	34	11.5	101	..	...	111	1	0.9
1947	206	3	1.5	135	..	...	52	..	...
1948	156	6	3.8	85	..	...	39	1	2.6
1949	689	36	5.2	292	1	0.3	237	..	...
Total	1,947	122	6.3	822	1	0.1	671	4	6.0

TABLE 2.—*Cases, Deaths, and Fatality Rates by Clinical Type and Year*

	Bulbar			Spinobulbar			Encephalitic		
Year	Cases	Deaths	Fatality Rate	Cases	Deaths	Fatality Rate	Cases	Deaths	Fatality Rate
1940	3	2	67.7	2	2	100	..	..	...
1941	21	7	33.3	5	3	60	1	..	...
1942	9	2	22.2	6	2	33.3	..	..	...
1943	..	..	.....	6	2	33.3	..	..	...
1944	49	7	14.3	49	10	20.4	1	1	100
1945	6	1	16.7	2	2	100	..	..	...
1946	42	13	31	38	17	45	3	3	100
1947	13	1	7.7	6	2	33.3	..	..	...
1948	14	2	14.3	15	3	20	3	..	...
1949	84	11	13.1	66	22	33.3	10	2	20
Total	241	46	19.1	195	65	33.3	18	6	33.3

DISTRIBUTION OF CASES AND DEATHS BY CLINICAL TYPE

It will be noted on examination of tables 1 and 2, which give the annual distribution of cases, deaths, and the fatality rates by clinical type, that there is a difference in the number of patients seen in the first half of the decade compared with the latter half. Prior to 1940, Detroit experienced an epidemic of poliomyelitis about every fifth to seventh year. In 1939 there were 521 reported cases in Detroit.

TABLE 3.—*Proportion of Cases and Deaths and Fatality Rates by Clinical Types*

	Patients		Deaths		
	No.	%	No.	%	Fatality Rate
Nonparalytic	822	42.2	1	0.8	0.1
Spinal	671	34.5	4	3.3	0.6
Bulbar	241	12.4	46	37.7	19.1
Spinobulbar	195	10	65	53.3	33.3
Encephalitic	18	0.9	6	4.9	33.3
Total	1,947	100	122	100	6.3

The next outbreak of considerable proportions was in 1944, and, except for a small number of cases in 1945, succeeding years had considerably more than the expected number. Deaths and fatality rates were also

*Controls were chosen by taking the first contact mentioned by the interviewed parent of the patient. A parent of the first contact mentioned was asked the same questions needed to record information on a special epidemiological form used for the patient.

irregular from year to year, reflecting the character of the disease as it occurred rather than any radical change in treatment. Thus, in 1944 there were 355 cases with 18 deaths compared with 295 cases and 34 deaths in 1946; in the latter year the proportion of bulbar and spinobulbar cases was decidedly higher than for 1944.

The proportion of cases and deaths by clinical type is noted in table 3, which also gives the group total fatality rates. The death recorded under the nonparalytic type occurred in a woman in her middle 30's in whom massive atelectasis developed while she was in the hospital. Although postmortem examination did not reveal the cause of the atelectasis, it is doubtful that poliomyelitis was responsible for the death. The fatality rate for the spinal type was expectedly low while higher center paralysis alone (bulbar) and in conjunction with spinal involvement (spinobulbar) and the encephalitic types, resulted in high fatality rates. The nonparalytic and spinal types are encountered most commonly, and fortunately the upper center types are less frequently noted. The encephalitic type was unaccompanied by any other involvement, while the bulbar and spinobulbar types did occur in a few cases with encephalitic findings. These will be placed in a separate category when refinements are made in future analyses of the data. The deaths are principally distributed between the bulbar and spinobulbar types, with the latter sharing the highest fatality rate with the encephalitic type but being much more important as a cause of death.

TABLE 4.—*Tonsillectomy in Relation to*

	Men											
	Nonparalytic		Spinal		Bulbar		Spinobulbar		Encephalitic		Total	
	Total	With Tonsillectomy	Total	With Tonsillectomy	Total	With Tonsillectomy	Total	With Tonsillectomy	Total	With Tonsillectomy	Total	With Tonsillectomy
1940	14	6	10	5	2	2	2	2	..	..	28	15
1941	20	9	17	9	14	14	5	3	1	..	57	35
1942	3	1	9	3	4	4	5	3	..	..	21	11
1943	..	..	15	7	..	..	4	3	..	..	19	10
1944	80	44	68	32	32	28	32	27	1	..	213	131
1945	13	4	3	2	2	2	..	..	..	..	18	8
1946	54	14	54	14	24	16	25	19	2	1	159	64
1947	89	41	28	14	6	5	3	1	..	..	121	61
1948	46	17	18	5	10	6	11	5	1	..	86	33
1949	175	80	139	49	51	44	41	23	10	5	416	201
Total	494	216	356	140	145	121	128	86	15	6	1,138	569

OCCURRENCE OF POLIOMYELITIS WITH RELATION TO PRESENCE OR ABSENCE OF TONSILS

The basic data relating to the presence or absence of tonsils and the occurrence of poliomyelitis are found in table 4, where the total number of patients in which tonsils have been removed at any time in life are given by sex, clinical type, and year. Although the proportion of patients with tonsils removed is not given for each category, it is readily apparent that there is variation from year to year in the nonparalytic and spinal groups and much less deviation in the higher center paralysis groups. With relation to sex, annual changes appear, but, when group totals are considered, the proportion of male patients who had tonsillectomies is 50% while for women it is 54.6% (not shown in table). The tonsillectomy rate for all cases is 51.9%, which is higher than the rate of 41.3% noted in 1939. Aycock [9c] reports a tonsillectomy rate of 33.8% among 2,857 cases reported by himself and others before 1942 and collected by him. Aycock estimated at the time of his studies the tonsillectomy status of the population was 30%, essentially the same as noted among the composite group of cases. This proportion is nearly the same as was encountered among the control group (26.7% with a history of tonsillectomy) in the 1939 Detroit study. It will be recalled that among cases at that time the rate was 41.3%. No data are available on the absence of tonsils in the general population for individual years in this study, but it is my opinion that it is considerably lower than 51.9%, the rate noted for the present study. It would be interesting to have this information for comparison purposes, but the differences exhibited in the proportion of cases after tonsillectomy by clinical type are sufficiently large to be statistically significant. If it were granted that the tonsillectomy status of the general population for the 10 year period was an average of 50%, one could still not discount the markedly high proportion of bulbar (85.1%) and spinobulbar (68.7%) cases in which tonsils had been removed at some time in life.

The data concerning deaths on the same basis are still more striking (table 5). From these data, which confirm and extend those cited by Aycock,[9c] it is obvious that patients with a severe type of poliomyelitis, or those who die as a result of this infection, are heavily weighted with respect to the absence of tonsils. This is illustrated by a comparison of Aycock's composite series and the Detroit experience (table 6).

COLOR, AGE, AND SEX DIFFERENTIATION

In 1940 the proportion of colored persons in the population was slightly over 9%, but by 1949 it had risen to over 16%. In this study the number of colored patients was 91 among a total of 1,947, a proportion of 4.9%. Only 4 of 122 persons who died were colored (3.4%). In both the case and death categories the colored patients fared better than the number expected from their population representation. The number of colored patients admitted to the Herman Kiefer Hospital was probably reduced somewhat by the fact that one of the hospitals admitting children through 12 years of age is situated in a predominantly Negro area and young children from that neighborhood would be more likely to be admitted

there. With respect to the fatality rate, the figure for colored persons was lower than that for white, being respectively 4.4 and 6.4. The difference is explained in part, at least, by the fact that 66.6% of the colored cases were nonparalytic, whereas among the whites the proportion of nonparalytic cases was 42.2%.

As with many other common infectious diseases, men are more commonly affected than women, and this is true of this study, though the difference is not marked. Men made up 58.4% of the total cases and accounted for 70.5% of the deaths. The marked difference in the proportion of deaths by sex is not readily explained unless one is willing to admit that stress, overstrain, and excessive fatigue are important predisposing factors and further that men are more often affected by them.

Table 7 reports on the number of patients that had undergone tonsillectomy and compares them by age groups. In addition, the proportion of cases by sex is given for each age group. With relation to numbers, the age groups 5 to 9 and 10 to 14 include more than 50% of the number of patients in each sex category. It is interesting that over the age of 20 years there were 103 men and 109 women, giving proportions of 18.1 and 24.7 for the respective groups. When the proportion of patients with tonsils removed is considered by sex and individual age groups, it is apparent that, with two exceptions, the men show the highest fraction in all age categories. In the 20 to 24 age group the proportion of women with tonsillectomies is 59.5% compared with 40.5% for the men. At the 35 to 44 age level, a small group, the proportion is the same for both sexes. The number and proportion of cases and deaths among patients with no tonsils as related to sex are shown in table 7. The number and proportion of male cases and deaths was again greater than for women. For patients, the proportion was 56.3, while for those who died it was 67.9. These figures match those for all cases and deaths regardless of the presence or absence of tonsils.

Type of Poliomyelitis, by Year and Sex

	Women											
	Nonparalytic		Spinal		Bulbar		Spinobulbar		Encephalitic		Total	
	Total	With Tonsillectomy	Total	With Tonsillectomy	Total	With Tonsillectomy	Total	With Tonsillectomy	Total	With Tonsillectomy	Total	With Tonsillectomy
1940	9	3	12	4	1	1	..	..	..	..	22	8
1941	13	5	18	5	7	4	..	..	..	..	38	14
1942	3	1	8	3	5	4	1	..	..	..	17	8
1943	2	1	12	4	..	..	2	1	..	..	16	6
1944	49	34	59	32	17	13	17	16	..	..	142	95
1945	3	2	1	..	4	4	2	2	..	..	10	8
1946	47	22	57	29	18	16	13	9	1	..	136	76
1947	46	21	29	16	7	7	3	2	..	..	85	46
1948	39	20	21	12	4	3	4	2	2	2	70	39
1949	117	50	98	44	33	32	25	16	..	..	273	142
Total	328	159	315	149	96	84	67	48	3	2	809	442

ELAPSED TIME BETWEEN TONSILLECTOMY AND POLIOMYELITIS

In this study the interval of time between tonsillectomy and the occurrence of poliomyelitis was studied at the following intervals: 1, 2 to 3, 4 to 6, and 7 to 12 months and by single years through 10, 11 to 15, and 16 to 20 years. For some persons, the time when tonsils were removed could not be specified, and these were placed under the column designated "No Information." Table 8 gives the elapsed time between operation and the disease by the above indicated periods and by clinical type. The literature available on the problem contains many reported studies relating to the high frequency of poliomyelitis following tonsillectomy within a period of one month. It is odd that in this 10 year experience of 1,927 patients only 21 should have had a tonsillectomy within one month of the attack of poliomyelitis. The 1939 experience gave a relatively low proportion in this respect, namely 5.1% for the cases, and the present study shows a lower figure, 2.1%. There are no controls in the present study as there were in 1939, and a comparison is therefore impossible on that basis as it was in 1939. Under one year, the totals for elapsed periods in months are as follows: 1 month, 21; 2 to 3 months, 24; 4 to 6 months, 18; and 7 to 12 months, 21. The first year accounts for 84 cases, a proportion of 8.3%. It is difficult to present a large amount of material in a table, for one has great difficulty in making a hasty mental assessment; but the information contained in table 8 is best handled in that manner, and careful scrutiny will show that for each clinical type the end sections of elapsed time contain the largest number of persons. In general, tonsillectomy is performed early in life, and this explains the high totals under the one, two, and three year periods. Essentially one-fifth of the patients with tonsils removed were over 20 years of age, and for most of them tonsillectomy had been performed in childhood. This accounts for the high totals at the 11 to 15 and 16 to 20 year intervals. The middle span of years from 4 through 10 show progressively smaller numbers, as would be expected considering age at tonsillectomy and the number of adults in the series.

COMMENT

The data presented above were obtained from careful history taking and direct examination of the patients involved. It comprises a large number of cases and covers a period of 10 years exclusive of the 1939 experience, which gave impetus to the present investigation. The proportion of persons admitted to the hospital with poliomyelitis who gave a history of tonsil removal is high for all clinical types encountered. The nonparalytic and spinal types most nearly approximate the level of absence of tonsils in the population at large. This is an estimate,

for no valid comparison of the occurrence of poliomyelitis among persons who had and had not undergone tonsillectomies was possible, particularly by single years over a period of a decade. Any one year's experience would be inadequate. In fact, in some of the clinical type categories, the number of cases is small and one would prefer larger numbers to gain significance. This study must be considered as one contribution to the body of information concerning the problem, and all evidence is not yet assembled for adequate consideration of the implications to the present moment; however, the findings here are in keeping with and supplement those of Aycock on the question of the occurrence of poliomyelitis with relation to the presence or absence of tonsils.

The explanation as to why removal of tonsils should produce more frequent higher center paralysis at an interval of a month or less of the operation is not difficult to understand in lieu of the pathogenesis of the disease and experimental work.[11] It is more difficult to find a reason for cases occurring at later intervals during the first year and for anytime thereafter in life. The value of tonsils to mankind has been a source of controversy for many years, although the multiple areas of lymphoid tissue that make up Waldeyer's ring and of which the tonsils are a part are considered to have some function relating to local immunity. It is possible that the removal of tonsils affects the portal of entry in some way or that their absence interferes with normal physiological mechanisms or the local immunity status of the mouth and posterior pharynx. Frankly, at this time, the significance of differences noted among persons with tonsils present or absent and the occurrence of poliomyelitis cannot be adequately explained for interval periods beyond one month.

TABLE 5.—*Deaths in Patients with Tonsillectomy at Any Time in Life by Clinical Type*

	Non-paralytic	Spinal	Bulbar	Spino-bulbar	Encephalitic	Total
Deaths	1	4	46	65	6	122
Patients who had had tonsillectomies, no	..	2	43	37	3	85
Patients who had had tonsillectomies, %	..	50	93.5	56.9	50	69.1

These data are challenging in their implications and call for sober judgment with regard to the desirability of tonsil removal except for excellent clinical indications. The nonremoval of tonsils may be as hazardous to a person or much more so than their removal, for the chance of contracting poliomyelitis in a clinically recognizable form is not great. Yet the data presented are strongly suggestive of a greater chance of contracting a severe form or of a fatal termination, if tonsils have been removed at some time prior to an attack of poliomyelitis.

SUMMARY

1. During the 1940-1949 decade, 1,947 patients who had had poliomyelitis were discharged from the Herman Kiefer Hospital. Among this group 1,011 patients gave a history of and on examination showed evidence of removal of tonsils. The proportion having undergone tonsillectomy was 51.9%.

2. High percentages of patients who had had tonsillectomy had the bulbar and spinobulbar types of poliomyelitis. The rates for these types were 85.1% and 68.7%, respectively, as compared to 45.6% for the nonparalytic and 43.1% for the spinal type. The fatality rate of 93.5% for the bulbar type when tonsils had been removed is still more striking and is in marked contrast to that for the spinobulbar type (56.9%).

3. The time elapsed between tonsillectomy and an attack of poliomyelitis was studied and the results were expressed by graded intervals. The proportion of patients with a history of tonsillectomy within one month of an attack was only 2.1% and for the period under one year, 8.3%.

TABLE 6.—*History of Tonsillectomy in Patients with Poliomyelitis, by Clinical Type*

Reference	Total Cases	Percentage with Tonsillectomy: Total Series	Non-paralytic Cases	Spinal Cases	Bulbar Cases	Spino-bulbar Cases
Aycock (seven series)	2,857	33.8	40.2	25.1	57.4*	....
Top	1,947	51.9	45.6	43.1	85.1	68.7

* Spinobulbar cases are included.

TABLE 7.—*Age, Sex, and Deaths of Poliomyelitis Patients Without Tonsils*

Age	Men: No.	Men: %	Women: No.	Women: %	Total No.
0- 4	25	73.5	9	26.5	34
5- 9	176	55.5	141	44.6	317
10-14	160	58.6	113	41.4	273
15-19	105	60.0	70	40.0	175
20-24	34	40.5	50	59.5	84
25-34	55	52.9	49	47.1	104
35-44	10	50.0	10	50.0	20
45+	4	....	..	....	4
Total	569	56.3	442	43.7	1,011
Deaths	53	67.9	25	32.1	78

TABLE 8.—*Period Elapsed Since Tonsillectomy and the Occurrence of Poliomyelitis by Clinical Type*

	Period Elapsed: Months				Years				
Clinical Type	1	2-3	4-6	7-12	1	2	3	4	5
Nonparalytic	6	3	8	10	46	41	47	24	25
Spinal	3	14	6	6	23	25	16	23	9
Bulbar	7	6	2	3	17	29	17	13	16
Spinobulbar	5	1	2	2	8	14	12	4	10
Encephalitic	..	..	..	..	..	2	1	..	..
Total	21	24	18	21	94	111	93	64	60

	Period Elapsed: Years								
Clinical Type	6	7	8	9	10	11-15	16-20	No Information	Total
Nonparalytic	30	19	9	8	18	33	38	10	375
Spinal	16	18	16	13	9	38	47	7	289
Bulbar	10	9	7	7	16	18	22	6	205
Spinobulbar	9	4	8	8	8	14	21	4	134
Encephalitic	..	..	..	3	..	2	..	..	8
Total	65	50	40	39	51	105	128	27	1,011

RELATIONSHIP OF TONSILLECTOMY TO INCIDENCE OF POLIOMYELITIS

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The question of the relationship of tonsillectomy to poliomyelitis has become more than a scientific one of virology or epidemiology and now involves problems dealing with the philosophy of medical practice. The pediatricians find themselves in a position similar to that of the otolaryngologists, since they are faced with the idea, supported in this case not by theory at all but only by statistics, that the routine immunization procedures that they have carried out may bring about an increase or, at least, a localization of paralysis. There is among their members, therefore, the same attitude that some otolaryngologists have shown: one almost of resentment that any such question should arise and interfere with their routine. Both these problems, like many others in the practice of medicine, resolve themselves into a matter of weighing one estimated risk against another. Any scientific discussion of this problem demands the knowledge and training of virologists, who should have a thorough understanding of the habits of the poliomyelitis virus, and epidemiologists, who can become very skilled in gathering significant mass data and in formulating statistical analyses. I am skilled in neither of these fields and am only a clinician. Therefore, I must make decisions on inadequate data, weighing one risk, partially known, against another risk, evaluated as best I can. In making any clinical decision, such as the proper time to do a tonsillectomy or to carry out an immunization procedure, such weighing and balancing must be made; but I believe that there should never be any question of weighing an identifiable risk to a patient against the convenience of the physician.

In general, there are two ways of arriving at an answer as to the importance or the actual existence of the tonsillectomy-poliomyelitis relationship. One approach depends upon theory. It must be considered whether, from what is known of the distribution of the virus and the pathogenesis of poliomyelitis, it should be expected that acute poliomyelitis might sometimes be consequent to tonsillectomy. The other approach depends on the actual collection of clinical data that would prove that such a sequence of events occurs and that it is a matter of cause and effect. Such data in this case must be collected under the handicap that the virus of poliomyelitis is not widespread, except in reference to the incidence of the disease itself, which, even in severe epidemics, is itself very infrequent. It is further made more difficult in recent years by the fact that there has been a great reduction in the number of tonsillectomies performed during the poliomyelitis season, so that the chance of a natural experiment presenting itself for analysis is reduced.

It has been established by previous studies,[1] using monkeys as experimental animals, that a polio virus placed in contact with the proximal end of freshly severed nerve trunks will invade the central nervous system by way of the axones of those nerves and set up first a localized and then a generalized reaction leading to typical disease, clinically and pathologically. It has not been established that this is the only path by which the virus can get into the central nervous system, but it is certainly one way, and there is much that leads one to believe that it may be a path commonly followed in man. Repeatedly, and by several workers,[2] a bulbar type of poliomyelitis has been produced in monkeys after tonsillectomy, usually most successfully when the operation is carried out immediately subsequent to the swabbing of the tonsillar area with virus. There seems to be no question of the possibility of imitating experimentally the clinical situation that is under discussion. It can therefore be said positively that there is ample theoretical grounds for understanding how a tonsillectomy can lead to a consequent attack of poliomyelitis if the operation is carried out at the time when the virus is in the throat. The virus is sometimes found in the throat, although it is found much more readily and persistently in feces. It is obvious, however, that, although the polio virus is relatively common in epidemic times, it is not common in nonepidemic times or areas, and even in severe epidemics not all members of the population are carriers of the virus. The new knowledge of the incidence of viremia after oral infection of monkeys with poliomyelitis does not change the importance of the original observations about the axone as a path for entrance of the virus to the central nervous system. If viremia does play an important part in the distribution of the virus to the central nervous system, the logical sequence to tonsillectomy in the presence of local virus in the throat could be viremia. Less clear-cut but highly suggestive and interesting evidence from animal experimentation would indicate that the stress of an operation itself to which a patient is subjected during an invasion period of the poliomyelitis, that is, when the virus is already in the central nervous system, may accelerate or aggravate the disease. This, of course, might apply to any traumatic experience equally well as to a tonsillectomy.

It can certainly be said that on the theoretical basis of present knowledge of the virus and its actions it might be expected and should be predicted that some cases of poliomyelitis would occur consequent to tonsillectomy. Now, in considering the direct evidence derived from clinical observations that such a relationship does occur, I will not review the many investigations and publications relating to the incidence of poliomyelitis in relation to tonsillectomy, as gathered from epidemiological studies. Some of the many such studies relate simply to a few cases in which circumstantial evidence points to this relationship, but where the evidence is not such as can be subjected to formal and accurate statistical analysis.

Read before the Joint Meeting of the Section on Laryngology, Otology and Rhinology and the Section on Pediatrics at the 101st Annual Session of the American Medical Association, Chicago, June 12, 1952.

1. Bodian, D., and Howe, H. A.: An Experimental Study of the Role of Neurones in the Dissemination of Poliomyelitis Virus in the Nervous System, Brain **63**: 135 (June) 1942.

2. Von Magnus, H., and Melnick, J.: Tonsillectomy in Experimental Poliomyelitis, Am. J. Hyg. **48**: 113 (July) 1948. Sabin, A. B.: Experimental Poliomyelitis by the Tonsillo-pharyngeal Route, with Special Reference to the Influence of Tonsillectomy on the Development of Bulbar Poliomyelitis, J. A. M. A. **111**: 605 (Aug. 13) 1938.

There have been more extensive studies of which a few might be mentioned by name: that of John Anderson in an epidemic in Utah,[3] of Gaylord Anderson from studies during an outbreak in Minnesota,[4] of Siegal in the New York 1949 season,[5] and of Dr. Cunning from data collected in various areas.[6]

TABLE 1.—*Bulbar Poliomyelitis in Poliomyelitis Cases with and Without Recent Tonsillectomy*

	Poliomyelitis			
	Bulbar, No.	Other Forms, No.	Bulbar, %	P*
0-10 years				
Tonsillectomy	24	12	66.7	.....
No tonsillectomy	771	6,063	11.6	<.001
3-7 years				
Tonsillectomy	12	4	75	.....
No tonsillectomy	96	395	19.5	<.001

* From chi square of differences between bulbar and other forms. In both series "P" indicates that probability of differences occurring by chance are less than 1 in 1,000.

Several types of data have been collected that seem significant. One is data that show that the bulbar type of poliomyelitis occurs more frequently after tonsillectomy than it does in the population at large. Another type of data indicates that the commonest interval between the operation and the disease is related significantly to the incubation period of poliomyelitis. A third type of data simply shows that the incidence of poliomyelitis in recently tonsillectomized patients, regardless of its type, is greater. Other evidence indicates that tonsillectomy at any time predisposes to poliomyelitis or to bulbar poliomyelitis, but such data are so hard to evaluate that I will not consider them.

I first became interested in the problem after seeing the patients that Dr. Aycock reported in one of the first observations on this subject.[7] This study was very small, but it was nevertheless very convincing. Of all the patients with poliomyelitis who had had tonsillectomy within a year before the disease, a striking proportion showed an interval of about one month or less between the operation and the disease, and a very high percentage of such patients had the bulbar form of the disease. An important observation of the tonsillectomy-poliomyelitis relationship was reported by Dr. Toomey [8] with subsequent viral studies and an epidemiological analysis of the patients involved by Francis [9] and others. This observation dealt with only a single family of six children but, nevertheless, because of the epidemiological studies and the actual demonstration of virus, was very convincing even though the group was small. In this natural experiment five children out of the six were subjected to tonsillectomy, and all five came down with bulbar poliomyelitis, three dying; a highly significant distribution of the virus of poliomyelitis was demonstrated.

Table 1 shows data presented by Dr. Faber [10] after his analysis of material from two sources. The first, from some of Cunning's work,[6] refers to children up to 10 years in which the incidence of the bulbar form of poliomyelitis and other forms is determined by those who had tonsillectomy within 30 days of the disease and those who had not had tonsillectomy. Here there is an incidence of 66 for the tonsillectomy group as compared with 11 for the nontonsillectomy group of bulbar patients. In the second series for children between the ages of 3 to 7 years, taken from Anderson's figures from Minnesota,[4] we have a relationship of 75 to 20, as between those who had tonsillectomy and those who had not. The data further show that these figures are statistically significant. Another type of data that include the incidence of the bulbar form of poliomyelitis as well as the total incidence of poliomyelitis is perhaps best characterized by the study of Dr. John Anderson in the 1943 epidemic in Utah. Table 2 shows a summary of his data again prepared by Dr. Faber.[11] The data are analyzed in two ways. First the number of tonsillectomies done in each of three summer months is indicated and the number of cases of bulbar poliomyelitis per thousand operations is recorded, there being as many as 19 cases per thousand in September. The same data than are reanalyzed in regard to the total child population and the total number of children who had tonsillectomies; here the incidence of poliomyelitis per 100,000 cases is approximately 2½ times as great in those children having tonsillectomy as in those without the operation and the incidence of bulbar cases is 16 times as great as in the general child population.

TABLE 2.—*Poliomyelitis Incidence in Cases of Recent Tonsillectomy*

	July	August	September
Tonsillectomies done	1,411	2,111	677
Bulbar or bulbospinal cases in 3-16 year age group preceded by tonsillectomy and adenoidectomy	1	3	13
Cases per thousand operations	0.7*	1.4*	19.2*

	Population	Polio-myelitis Cases	Polio-myelitis Incidence per 100,000	Bulbar Cases	Incidence of Bulbar Cases per 100,000
General child population	156,000	232	152*	39	25*
Children with tonsillectomy	4,199	17	404*	17	404*

* Calculated from the data as given by Anderson.

Now, in contradistinction to the many studies that show a relationship between tonsillectomy and poliomyelitis are those of Dr. Cunning, which were presented to you in a series of annual reports before the American Laryngological, Rhinological, and Otological Society.[6] In Dr. Cunning's conclusions he states that he finds no relationship between tonsillectomy and poliomyelitis. Incidentally, in his conclusions he and other observers are not so far apart, since Dr. Cunning recommends on

3. Anderson, J. A.: Poliomyelitis and Recent Tonsillectomy, J. Pediat. **27**: 68 (July) 1945.
4. Anderson, G. W.; Anderson, G.; Skaar, A. E., and Sandler, F.: The Risk of Poliomyelitis After Tonsillectomy, Ann. Otol., Rhin. & Laryng. **59**: 602 (Sept.) 1950.
5. Siegel, M.; Greenberg, M., and Magee, M. C.: Tonsillectomy and Poliomyelitis: Studies on Incidence in 1949, J. Pediat. **38**: 537 (May) 1951.
6. Cunning, D. S.: Tonsillectomy and Poliomyelitis, Arch. Otolaryng. **46**: 575 (Nov.) 1947. Tonsillectomy-Poliomyelitis Survey-1947, Laryngoscope **58**: 503 (June) 1948. Poliomyelitis-Tonsillectomy Survey-1948, Laryngoscope **59**: 441 (May) 1949.
7. Aycock, W. L., and Luther, E. H.: Occurrence of Poliomyelitis Following Tonsillectomy, New England J. Med. **200**: 164 (Jan. 24) 1929.
8. Krill, C. E., and Toomey, J. A.: Multiple Cases of Tonsillectomy and Poliomyelitis, J. A. M. A. **117**: 1013 (Sept. 20) 1941.
9. Francis, T., Jr.; Krill, C. E.; Toomey, J. A., and Mack, W. N.: Poliomyelitis Following Tonsillectomy in 5 Members of a Family: Epidemiologic Study, J. A. M. A. **119**: 1392 (Aug. 22) 1942.
10. Faber, H. K.; McNaught, R. C.; Silverberg, R. J., and Dong, L.: Experimental Production of Post-Tonsillectomy Bulbar Poliomyelitis, Proc. Soc. Exper. Biol. & Med. **77**: 532 (July) 1951
11. Faber, H.: Adenotonsillectomy and Poliomyelitis, Pediatrics **3**:255 (Feb.) 1949.

several occasions that elective tonsillectomies should not be carried out during an epidemic of poliomyelitis. His data are honestly and painstakingly collected. Although he states in conclusion that no relationship is found, actually in some of his data, as analyzed by Dr. Faber, there is evidence of almost twice the incidence of the bulbar form of poliomyelitis in those who have had tonsillectomy within two months before the disease than in patients who have not had tonsillectomy.

Again I must state that I am not a statistician and will not attempt to give an authoritative explanation of this difference, but it seems to relate to the way his data were collected; the usual criticism of Dr. Cunning's work is that he diluted his figures too much, and, in fact, a large volume of data can actually conceal evidence apparent in more critical collections. Thus Dr. Cunning may have succeeded only in showing that poliomyelitis itself is rare, as actually it is. If the incidence of poliomyelitis in New York is considered during an epidemic year, such as 1949, the year that Dr. Siegal used for one of his studies, it is shown that the case rate was only 1 in 3,000 inhabitants of the city. If we assume that only a quarter of the total population is presumably susceptible to poliomyelitis, then we would have a case rate among that group of 1 to 750. If we assume that of that case rate as much as 15% were the bulbar type, then we would have a bulbar poliomyelitis case rate among the susceptible group of 1 to 5,000. If tonsillectomy increased the risk to bulbar poliomyelitis by only 10 times, a physician should still see only one case in 500 tonsillectomies. This, of course, is all speculative playing with numbers but does give some idea of the reason why the experience in one's personal private practice can hardly be a basis for evaluating this risk. Since the virus of poliomyelitis is not ubiquitous, even though it is relatively widespread in epidemic times as compared with the actual incidence of the disease, it is clear that simply collecting volumes of data in nonepidemic areas or in nonepidemic years on poliomyelitis patients or patients who had had tonsillectomies may not reveal any significant relationship. Thus the incidence of poliomyelitis owing to tonsillectomy in any epidemic, as estimated by many observers, is still so small in total that the addition of other data, collected from areas where the virus is not common or not present, makes the evidence of this relationship quite fade away and the significant figures disappear. Even though the over-all risk thus becomes quantitatively small, and in national figures probably undetectable, the more intense risk in any epidemic cannot lightly be considered negligible.

I personally believe that there is a very important causal relationship between tonsillectomy and bulbar poliomyelitis and that a tonsillectomy in certain circumstances may greatly increase the risk of a fatal disease; but let us assume that the matter is still in question, that there is still doubt of it, but that all the conflicting data are equally respectable. Since there is every theoretical reason to believe such a relationship might occur and since an unsettled question implies a risk, as a clinician I must assume that an actual risk, even though small, is involved in doing a tonsillectomy in the poliomyelitis season. As a clinician I do not feel that it is necessary to wait for evidence of such increased risk to be expressed in dependable quantitative terms before I take some action. I can only ask what the risk is of postponing the tonsillectomy and then try to weigh one risk against the other.

1313 E. Ann St.

THE UNITED STATES PUBLIC HEALTH SERVICE'S CLINICAL CENTER FOR MEDICAL RESEARCH

Norman H. Topping, M.D., Bethesda, Md.

The interrelationships between clinical medicine and medical research form one of the most intriguing chapters in the history of medicine. They have never been completely separated, or completely together, and the ways in which they have affected each other have varied markedly as medicine has evolved in this country. During recent years, perhaps as a cumulative effect of the general lifting of standards of medical education since the Flexner report, the spirit of inquiry has been widely dispersed among practicing physicians. Indeed, the innumerable studies and observations made in the course of medical practice are an indispensable contribution to the total medical research effort of the nation.

At the same time, the scope of laboratory research related to medicine has expanded rapidly as the techniques and viewpoint of the biochemist and biophysicist have been brought to bear not only on disease problems but on the mechanism of normal body function. Few, however, would claim that clinical medicine and research are now related in an ideal way. Within the laboratory, specialization has reached a point where synthesis of ideas across the boundaries of limited fields is becoming difficult. The same can be said of clinical specialization. In addition, it has become apparent that the observations and investigations of clinicians are sometimes deficient because the basic requirements of sound research are not or cannot be observed.

One of the major challenges of medicine in the years ahead will be to work out the mechanisms and relationships that will permit the abundant clinical and laboratory talent of the nation to work most productively together for the welfare of man. The National Institutes of Health faces this challenge together with other medical research organizations. The form that the problem takes is a reflection of the organization and its functions.

Structurally, the National Institutes of Health is composed of seven institutes, whose names indicate their general area of interest—National Cancer Institute, National

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Read in the General Scientific Meetings at the 101st Annual Session of the American Medical Association, Chicago, June 9, 1952.

Assistant Surgeon General, United States Public Health Service; Associate Director, National Institutes of Health.

Heart Institute, National Institute of Arthritis and Metabolic Diseases, National Institute of Dental Research, National Institute of Mental Health, National Institute of Neurological Diseases and Blindness, and National Microbiological Institute. The National Institutes of Health is the principal research arm of the Public Health Service, which is in turn a part of the Federal Security Agency. Each component institute has two important missions—research in its own laboratories and administration of grants and fellowships to aid medical and related research elsewhere. My associates and I consider our research grant and fellowship activities, which are more widely known to university persons than to practicing physicians, to be of major importance. The grants that we administer support between 20% and 25% of all research undertaken in medical schools. We are conscious that our policies have a significant bearing not only on medical research but indirectly on medical education.

Our actions are guided by two fundamental principles: First, we leave those who receive grants free to pursue their own ideas with no federal control or supervision whatever. Second, we rely heavily on the advice of seven National Advisory Councils established by law and on the counsel of 19 technical groups called Study Sections. Both groups are composed largely of nonfederal experts forming a cross section of the best the nation affords in clinical and laboratory research talent. We attribute the effectiveness and wide acceptance of the grants programs largely to these fundamental policies and to the guidance we receive from our advisers.

RESEARCH PROGRAM

As far as research in our own laboratories is concerned, we have concentrated almost exclusively on basic laboratory research. This work covers virtually every discipline related to medicine. We devote a good deal of attention, for example, to enzyme chemistry, genetics, immunology, electron microscopy, tissue culture, pathology, and endocrinology. Work in these areas is usually, but not always, related to a specific disease problem. In our opinion, the key to many diseases that are of increasing importance will be found in research of this type. Investigations bearing on public health as traditionally conceived—milk and water sanitation, applied epidemiology, air pollution, and public health administration, for example — are carried on largely in the Communicable Disease Center and the Environmental Health Center of the Public Health Service.

The great gap in this research program has been in clinical research. We have been hampered for a number of years by inability to carry our laboratory findings through to clinical evaluation. We have also been hampered to an unknown but important degree by the absence of the stimulus that clinical research offers to laboratory research.

The first tangible step toward the addition of a substantial volume of clinical research to our program was taken a few years ago with the appointment of a committee by the Surgeon General of the Public Health Service to lay out general guide lines. This group and its descendants have formulated some broad principles that have shaped all subsequent decisions. One of the first decisions was that a separate clinical facility was needed and that it should be an adjunct to research, rather than part of the Public Health Service's other hospital activities. A most significant corollary to this decision was that high quality patient care should never be subordinated to research, even though the facility was essentially an adjunct to research.

We decided that our objective would be to bring together in close physical and intellectual proximity the full array of high caliber laboratory and clinical investigators required for a broad attack on medical and related problems. We firmly believe that collaborative effort of this sort is a pattern that can contribute in a unique way to the advancement of medicine. The difficulties of such an enterprise are obvious, and a large share of our subsequent planning for physical facilities and for organizational relationships has been directed toward the translation of the general objective into reality. Finally, we came to the conclusion that our facilities should be considered as a national resource, and not simply a Public Health Service laboratory. To carry out this principle we determined to invite outstanding persons from this country and abroad to work with us as visiting scientists.

PHYSICAL PLANT

In 1947 Congress unanimously voted for construction of a clinical center for coordinated laboratory and clinical investigation of a wide spectrum of diseases. Over the next two years, we evolved a plan for the building itself which seemed to reconcile the practical with the ideal. During that period, our scientists, engineers, nurses, dentists, and administrators consulted extensively with clinicians, investigators, hospital administrators, and laboratory designers from other institutions. The end product was a laboratory-hospital building, which will allow laboratory investigators and clinicians to work closely together and also will meet the ever-changing requirements of laboratory research, patient care, and administrative practices.

As far as patient care facilities are concerned, the Clinical Center will have 500 beds, all of which will be solely for research patients. The beds have been allocated tentatively among our several institutes about as follows: heart, 104 beds; cancer, 126 beds; mental health, 98 beds; arthritis and metabolic, 78 beds; neurology and blindness, 42 beds; and microbiology, 52 beds.

When it opens in April, 1953, the Center will have the usual resources of a modern general hospital, including ancillary services such as physical medicine and rehabilitation, medical and psychiatric social work, recreational therapy, and spiritual ministry. The patients' rooms and nursing and medical services are designed to provide maximum comfort to the sick and working convenience to the staff. There will be a chapel, auditorium, post office, bank, cafeteria, and other facilities for the convenience of patients whose average stay is expected to be considerably longer than is the case in most hospitals.

A follow-up department will handle returning patients and special studies involving examination of normal controls, ambulatory patients, and similar functions directly related to the research program. An outpatient department, in the usual sense of the term, is not contemplated.

The average teaching and research hospital devotes about twice as much space to patient care as to research. This ratio is reversed in the Clinical Center. The high ratio of laboratory to patient care space is also a reflection of our intention to continue stressing fundamental study. Modular space design with movable partitions provide the flexibility that has been found essential in modern laboratories. The laboratories are, in general, of two types—clinical and nonclinical.

Clinical research laboratories are on the north side of the main stem, immediately adjacent to the patient care facilities on the south side of the main stem. Basic science laboratories are in the six wings. Corridors are arranged so as to separate completely from patients and the patient care staff the traffic involved in research activities.

The nonclinical laboratories, which are in effect an extension of our existing laboratory facilities, will be in wings off the main stem. One of these wings has been specially designed and equipped for research and therapy utilizing various forms of radiation. Centralization of this function is, in our opinion, conducive to more effective employment of these techniques and permits a greater degree of safety to patients and staff. We will have small laboratory animals, such as mice, guinea pigs, hamsters, and rabbits, in the nonclinical laboratory wings. Work with larger animals will be done in other buildings.

In order to permit the most effective use of the relatively expensive space in the Clinical Center building itself, some activities will be carried on in outlying buildings. Machine shops, the laundry, power plant, bulk storage, and animal breeding are some of these.

We intend to observe the operation of the Clinical Center closely and to use it as a laboratory for studying problems outside the field of biology and medicine. The Center in operation will provide a useful site for examination of techniques of hospital administration, utilization of subprofessional personnel, sanitary engineering, and food and garbage disposal, and means of handling and disposing of radioactive materials.

SELECTION OF PROBLEMS

As these plans for the physical layout progressed, we gradually formulated our operating policies in greater detail. One of the most significant of these relates to the selection of areas of research in medicine and biology. Selection of problems for study will be guided by a principle long observed at the National Institutes of Health, which holds that scientific research flourishes and is productive only in an atmosphere of intellectual freedom. Therefore, the acceptance or selection of problems for investigation, the design of the experiment, and the methods to be employed are the prerogatives of responsible staff scientists free from pressure, authoritarian direction, or control from above or outside.

In addition to basic studies in clinical medicine, much of the clinical work will be to evaluate clinically laboratory findings. Other clinical studies will attempt to validate procedures developed elsewhere but inadequately tested. We are convinced, however, that the volume of such work must be kept relatively small if the Clinical Center is to be an outstanding research institution.

As a publicly supported medical research institution, we are often urged to test various theories and remedies arising from the extraordinarily fecund imagination of lay persons, and occasionally from professional persons not familiar with current knowledge in a particular research field. Out of this long and sometimes rather harassing experience we have evolved three criteria that must be met before we can consider such proposed evaluations. Reduced to their simplest terms, these criteria are as follows: 1. The method of treatment must be fully explained—there must be no secrecy in regard to procedure or the composition of drugs used. 2. Diagnoses must have been made by a physician. Patients must have been treated and records kept under supervision of a physician. Complete records of patients treated must be submitted. 3. Clinical records must show that the patients were cured by the treatment described and that no other form of treatment was used.

RESEARCH PATIENTS

An overriding principle governing our clinical studies is that the welfare of individual human beings takes precedence over every other consideration. Medical procedures or therapy substantially different from accepted general medical practices are often an essential component of clinical medical research. This offers the only means of acquiring certain information necessary to solve the problems of the diseases and disorders that afflict man. Ethical and scientific considerations dictate, however, that these investigations must be undertaken only after mature thought, under rigorously defined and controlled conditions, and under circumstances that will minimize the dangers of predictable or unpredictable hazards. The basic principle on which all such investigations must rest is that human beings have inalienable rights that supersede all other considerations that may be raised in the name either of science or of the general public welfare. The responsibility of the physician for the physical and mental well-being of persons in his care and for observance of the ethics of his profession cannot be overridden by any element of study or research that is interjected into the relationship between the physician or surgeon and persons in his care.

We will, therefore, give each research patient as good medical care as he would receive in any of the nation's best general hospitals. The procedure of patient care, the physical arrangements, numbers and kinds of physicians, nurses, and technicians, and their facilities are being discussed and planned with this goal in mind.

The staff who will have direct charge of patients as members of the central staff and those who will direct the clinical studies of each of the institutes sharing the clinical center will be of high caliber. In selecting the medical staff and other key persons we have consulted widely with medical school deans and heads of departments, hospital directors, and the like. Almost without exception, even when it meant the possibility of losing a valued associate, they have shown great interest in our goals and have aided our recruitment efforts.

One problem to which we have given a great deal of thought and discussed most frequently is whether our patients should be required to pay. The medical care

received during a research study is a necessary adjunct and not the primary purpose of the Clinical Center operations. By becoming a participant in medical research the patient is making an important contribution to the advancement of knowledge. Frequently, the volunteer participant in clinical studies must also undergo considerable inconvenience and discomfort. Of equal importance is our conviction that we could not obtain the number of patients with precisely the characteristics needed for our various studies just when they were needed if they had to pay for hospital, medical, and surgical care. Therefore, we have decided that it would not be proper to require the patient to pay. Those patients who, of their own volition, wish to make a gift out of personal gratitude will be permitted to do so as a right and not as an obligation.

Investigators will select patients on the basis of potential value to their studies. Patients will be admitted to the Center only on appropriate medical referral after a preadmission examination to establish that his precise diagnosis and other characteristics make him a fully suitable subject. Arrangements for referral will be negotiated with individual physicians, or with hospitals, clinics, and similar institutions. While diagnosis is the primary criterion, other factors will be considered in the selection of patients. Among these are (1) the adequacy of the subject for concurrent studies; (2) possibilities for follow-up study, including such factors as ease of return or readmission, or the interest of the patient's own physician in giving follow-up examinations; (3) probability of patient and sponsor cooperation before, during, and after the period of active study; and (4) the confidence of the Clinical Center staff in the reliability of the referring organization or individual physician. Under these policies the Center will not become a home for incurables or a convenient place to obtain hospitalization at the taxpayers' expense.

Full reports on each patient will be given at suitable intervals to the referring physician or institution, and the receipt of similar pertinent reports will be welcomed. Active collaboration between the patients' own physician and the Clinical Center staff will be essential for interim therapy and observation. Referring physicians will be welcome to visit the Center and to confer with the appropriate staff members and consultants.

STAFF

The medical care staff in the Clinical Center will be organized as in any general hospital. This staff will work under the supervision of the Clinical Center Director, who has sole responsibility for services concerned with the general welfare of the patient. The Clinical Center director, in turn, is responsible to one man—the director of the National Institutes of Health. The clinical studies in which the patient participates will be the responsibility of the chief of clinical research of the particular institute initiating the study. These clinical chiefs will also serve as a medical board to advise on broad policies governing medical care in the Center.

Staff physicians who will be concerned with medical care or services directly related to medical care and those who will do clinical research are being recruited throughout the country. Naturally, we are trying to get the best persons available. The prospects for concentrated research, the atmosphere of scientific freedom, and the good facilities are enabling us to obtain an outstanding staff despite the relatively low federal salary scale.

On our present staff there are about 125 clinicians competent in such fields as internal medicine, surgery, neurology and psychiatry, radiology, and pediatrics. We expect to add about 30 new clinicians during the first year of operation and 30 more during the second year. In the preclinical medical disciplines, such as anatomy, bacteriology, biochemistry, and pathology, our present staff strength is about 120. By the end of our second full year of operation we hope to add 30 to 40 to this group.

In numerous discussions with medical school deans and hospital directors on the subject of staff recruitment, we have emphasized that the Clinical Center will be a national resource. In homelier terms, the National Institutes of Health is a two-way street—while nonfederal institutions are losing good men to us, they are receiving other good men from us.

This exchange has been going on for many decades. One recalls among other instances that McCoy left the National Institutes of Health to become dean at Louisiana State University Medical School, Rosenau to become professor of preventive medicine at Harvard, Maxcy went to the professorship of epidemiology at Johns Hopkins, Victor Heiser to the Rockefeller Foundation, Mansfield Clark to professor of chemistry at Hopkins, and R. E. Dyer became director of research at Emory's Winship Clinic.

This interchange of persons with special skills and fresh viewpoints will be carried even further in the Clinical Center under our visiting scientist and research fellowship programs. Already well established at the National Institutes of Health, these programs enable both distinguished "elder statesmen" of science and brilliant young research students to work in our laboratories for periods of a few weeks to several years and then to go back to their parent institutions. Within the past few years, for example, three Nobel Prize winners in medical research have worked with us, one for several months and the others for more than a year.

We have set aside substantial funds and laboratory space for these visiting scientists. On invitation from us, an able, established scientist from another institution may work in the Clinical Center on problems of his own choosing. We will furnish space, equipment, technical help, professional collaboration, and the intellectual stimulation of constant association in a research climate with other distinguished colleagues. The visitor will, of course, publish his findings where and when he prefers.

The laboratory research fellows in the Clinical Center will be financed as is now the case, not only under our fellowship program but by various nonfederal fellowship plans. We always have a number of predoctorate fellows working at the National Institutes of Health on theses for fulfilment of Ph.D. degrees granted by universities.

The general policies that will govern clinical research training in the Center, corresponding to residency train-

ing elsewhere, derive from our threefold purpose of adding materially to the body of useful scientific knowledge concerning the diseases of man, of helping build the medical and research manpower of the nation, and of providing the best possible medical care. Within these terms we feel that the training offered clinical fellows should represent primarily those elements that are unique or that represent the highest form of skill that can be imparted by the Clinical Center group.

We naturally feel that clinicians trained in the Center should secure proper recognition by the appropriate specialty boards, and arrangements for this recognition are progressing satisfactorily. Each of the institutes will prefer to offer a clinical fellowship program directly related to its principal field of interest. However, each will accept fellows having primary interest in certain other fields, provided approval can be obtained from the particular board concerned. It is our belief that we will have outstanding resources to meet board requirements for broad exposure to research and the basic sciences. Formalized, didactic training will be available through suitable arrangements with nearby universities. When in full operation we estimate our facilities will be adequate for somewhere between 40 and 60 clinical fellows, or a ratio of 7 to 15 beds per fellow.

We anticipate need for consultants in a number of special fields—allergy, urology, maxillofacial surgery, otolaryngology, and gynecology are a few that come to mind. We plan to appoint consultants from centers of medical leadership in all sections of the country, who will serve in situations ranging from regular visits and ward rounds to a single visit to see a particular patient.

The deans of the seven nearby medical schools of Maryland, Virginia, and the District of Columbia have agreed to assist in developing panels of local consultants. They have also given invaluable counsel on many other topics. The keen interest shown by these local deans and by literally hundreds of other leaders in medicine in every

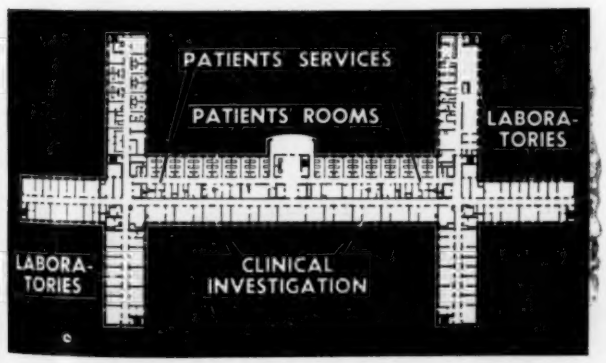

Fig. 1.—A typical floor plan of the Clinical Center.

part of the nation has greatly encouraged and helped us during the difficult days of planning and building the Clinical Center. It has also caused us to believe more firmly than ever that our plans will help meet a need that is widely recognized among the leaders of medicine, public health, and the basic sciences.

Reduced to its simplest terms, medicine and the laboratory sciences have grown indispensable to each other; at the same time each has become so intensively specialized that effective communication between the two broad fields, and between the numerous specialties within each, has become inordinately difficult. Man cannot devise a more desirable and effective system of communication than the direct, face-to-face method. The Clinical Center will provide a means for bringing together in constant

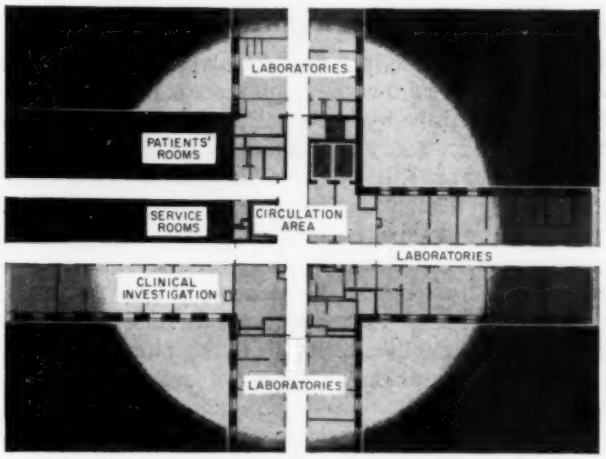

Fig. 2.—Circulation area of the Clinical Center. Coordination of the patient—clinical investigation—laboratory operations.

intellectual and physical contact outstanding practitioners in virtually all the clinical and laboratory specialties. This will be done in the presence of that most powerful inciter of creative thought—the sick human being for whom the vast potentialities of medical science have not yet been realized.

The ultimate purpose is to help provide the practicing physicians of this nation—and of the world—with better means for ameliorating physical suffering and emotional imbalance, for prolonging human life, and for making all the years of that span more useful both to the individual and to society.

Anesthetic Deaths.—One of the most common causes of anesthetic deaths is nursing the unconscious patient in a faulty position. The problem is one of simple mechanics. With the patient lying on his back, if the jaw is left unsupported, the tongue will fall back and occlude the airway. This is an elementary fact which generations of instructors in anesthesia have drilled into their students over and over again. When the operation ends, this danger remains unchanged. And yet, for some unknown reason, the anesthetist may turn over the unconscious patient to an attendant who puts the patient flat on his back in bed and leaves him unsupervised, often for considerable periods. There is only one way to nurse an unconscious patient. He should be placed in a semiprone position, with a firm pillow under the chest to prevent him from rolling onto his face, and his lower arm should be drawn behind him to insure that he will not roll onto his back. In this position, the tongue falls away from the posterior pharyngeal wall, and a blood clot, vomitus, or any foreign body drains out of the mouth and not into the larynx. It is a very good position, especially for patients recovering from tonsillectomy, laparotomy, or practically any other operation. In this position, the patient who has been deprived of his protective reflexes is the moral responsibility of the anesthetist. Of course, the anesthetist cannot stand by each patient until he recovers but, in delegating his responsibility, he should insist that the patient be placed in a safe, prone position.—C. Brudzynski, M.D., Investigation of Anesthetic Deaths, *Annals of Western Medicine and Surgery*, August, 1952.

who will do clinical research are being recruited through- training in the Center, corresponding to residency train-

THERAPEUTIC EXPERIMENTS IN ALOPECIA AREATA WITH ORALLY ADMINISTERED CORTISONE

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A recent clinical and statistical study of 230 patients with alopecia areata, including the totalis and universalis varieties,[1] revealed that although there is no evidence of endocrine abnormality in this disease, hormonal factors may play an accessory or modifying role in its course. It was found that (*a*) the course of alopecia areata is much severer when it begins before puberty; (*b*) some patients with alopecia totalis recover completely during pregnancy and lactation; and (*c*) some patients with alopecia areata have their onsets simultaneously with thyrotoxicosis. It was thought that endocrine substances may exert their modifying influence indirectly by altering the soil upon which the unknown causative agent of alopecia areata acts.

With the advent of corticotropin (ACTH) and cortisone and after the report on the dramatic therapeutic effect of these hormones on rheumatoid arthritis,[2] which, like alopecia areata, often shows considerable improvement during pregnancy, it seemed to be justified to study the effect of these hormones on the course of alopecia areata. This present paper is a report on 22 patients who received treatment with orally administered cortisone acetate.

PRELIMINARY FINDINGS

Selection of Patients.—In the early stage of this study, only those patients were taken into the experiment in whom spontaneous regrowth of hair was not to be expected, i. e., patients with alopecia totalis or universalis of at least two years' duration. Later, when it became apparent that administration of cortisone actually produces hair growth that cannot be confused with spontaneous recovery, persons with less severe cases and with cases of shorter duration were also included. Meanwhile, it became clear that patients with long-standing alopecia, 10 years or more, are less likely to respond to therapy.

Eleven of the 22 patients had alopecia universalis (or nearly universal), 4 had alopecia totalis (or nearly total) of the scalp, and 7 had patchy loss of hair on the scalp (alopecia areata). Five patients of the latter two groups also had patchy hair loss elsewhere than the scalp. Twelve patients were female and 10 were male. The ages ranged from 12 years (two boys) to 57 years, with the average age being 28.4 years. The diagnosis was established by history and clinical examination. All patients had the characteristic clinical picture of hair loss either in circular patches or generalized, with clinically normal skin and normal follicular pores in the bald area and with no atrophy and no scarring. None of the patients had any demonstrable systemic disease. Eighteen patients gave a history of the alopecia having started with growing circular bald patches. Two, however, had a rapidly progressing, diffuse hair loss without ever noticing round bald patches. Two patients could not remember how the balding process started in childhood.

Course of Disease Prior to Therapy.—In 16 patients the alopecia was stationary at the time therapy was initiated; in five others the baldness was progressing. One patient noticed slight regrowth of hair shortly before treatment was started. In all patients the duration of the last attack without any sign of improvement prior to therapy ranged from three months to 20 years, the average being 6 years and eight months.

Spontaneous complete remission occurred in four patients prior to therapy, one remission in each case. Two of these coincided with pregnancy. In the two other cases the remission, which could not be linked with any event, lasted for 2 and 22 years respectively. One patient reported considerable improvement but no complete remission during pregnancy. Another patient experienced no improvement during pregnancy and later did not respond to cortisone therapy either.

THERAPY

All 22 patients were given cortisone acetate (Merck) tablets orally after general physical and routine laboratory examination, including chest microfilm, complete blood counts, Kahn's reaction, and urine analysis. All patients while under treatment were asked to add no salt to their food at cooking or at the table. All received potassium chloride, 0.3 to 0.9 gm. daily, depending on the amount of cortisone administered. While patients were taking 75 mg. daily or more of cortisone, they were seen weekly; otherwise, less frequent observation was permitted. All patients were weighed at each visit, thus giving us a clinical index of water retention.

The initial drug dosage was 100 or 150 mg. daily (in three or four divided doses) according to body weight and/or severity of the disease. This dosage was continued for four weeks or longer. However, when hair growth was progressing well, the quantity was gradually lowered in an attempt to establish the minimum maintenance dosage that would promote continuation of active

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Dr. George C. Wells made the study and interpretation of the histopathological material used in this study.

A preliminary report of this study was published in *The Journal of Investigative Dermatology* (**18**: 5 [Jan.] 1952).

A portion of the cortisone acetate used in this study was supplied by Dr. Elmer Alpert, Merck & Co., Inc., Rahway, N. J.

Read before the Section on Dermatology and Syphilology at the 101st Annual Session of the American Medical Association, Chicago, June 11, 1952.

This work was supported in part by an institutional research grant from the American Cancer Society and in part by a grant from the United States Public Health Service.

1. Walker, S. A., and Rothman, S.: Alopecia Areata: A Statistical Study and Consideration of Endocrine Influences, J. Invest. Dermat. **14**:403 (June) 1950.

2. Hench, P. S.; Kendall, E. C.; Slocumb, C. H., and Polley, H. F.: The Effect of a Hormone of the Adrenal Cortex (17-Hydroxy-11-Dehydrocorticosterone: Compound E) and of Pituitary Adrenocorticotrophic Hormone on Rheumatoid Arthritis: Preliminary Report, Ann. Rheumat. Dis. **8**: 97 (June) 1949.

hair growth. Attempts to induce hair growth with initial doses lower than 100 mg. per day have failed. In two cases the administration of 37 mg. daily and in one case the administration of 75 mg. daily were unsuccessful; however, when 100 mg. was given daily, new hair growth was observed in two of these three patients later.

Maintenance Dosage of Cortisone.—In all patients the medication had to be continuous. Cessation of therapy or decrease of the dosage below a certain critical level invariably resulted in a relapse. The newly grown hair loosened and fell out, and regeneration stopped. In six patients the treatment to date has been continued long enough to establish the effective maintenance dosage. This was done by gradually lowering the drug amount until either the newly grown hair started to loosen or the dosage was at a level of 25 to 37 mg. daily. Two patients were maintained on 25 and 37 mg. daily doses respectively, each for a period of three months, with hair growth progressing at a normal rate. Later on, however, these two patients, along with the other four, required 50 to 75 mg. of cortisone daily for maintenance. At present, three patients are maintained on 50 mg. and three on 75 mg. daily. One patient with universal alopecia who responded well to the initial high dosage lost his newly grown scalp hair (except for two poorly growing tufts) when the dosage was reduced to 12.5 mg. daily. Two other patients who responded well to initial treatment rapidly lost all newly grown hair when therapy was discontinued.

THERAPEUTIC RESULTS AND FINDINGS

Hair growth occurred in 16 out of 22 patients. The growing hair became visible three weeks after initiation of treatment in 4, during the fourth week in 10 patients, and after six weeks in 2. In no patient so far observed has the regrowth been complete. (Detailed results are shown in table 1.) Fifteen patients showed regrowth of hair on the scalp, six displaying a diffuse growth and nine a patchy growth of hair. All these patients also had regrowth in other areas than the scalp, such as eyelashes, eyebrows, beard hair, and body hair in varying degrees; however, the regrowth was never complete. One patient with alopecia universalis regrew eyelashes only. In only three instances was there partial regrowth of axillary and pubic hair. It was our impression that, independent of duration and severity of this disease, these two areas were most resistant to the effect of cortisone. In the course of cortisone administration three patients experienced the development of new patches or the enlarge-

TABLE 1.—*Alopecia Patients Showing Regrowth of Hair Following Cortisone Therapy*

Case	Sex	Age	Age at Onset	Type of Alopecia	Duration of Last Attack, Yr.	Active Disease Throughout Puberty	Regrowth		Cosmetic Result
							Patchy	Diffuse	
1	F	15	15	Areata	⅜	No	X	..	.....
2	F	57	55	Totalis	1½	No	..	X	.....
3	F	27	24	Totalis	¼	No	X	..	.....
4	F	21	10	Areata	2	No	..	X	Satisfactory
5	M	27	22	Areata	5	No	..	X	Satisfactory
6	F	40	26	Areata	14	No	X	..	.....
7	F	48	40	Totalis	8	No	X	..	Unsatisfactory
8	F	37	25	Areata	7½	No	..	X	Satisfactory
9	M	12	10	Universalis	2	No	X	..	.....
10	M	34	24	Universalis	10	No	X	..	Unsatisfactory
11	F	14	11	Universalis	2½	No	X	..	.....
12	M	30	8	Universalis	¾	No	X	..	.....
13	M	35	26	Universalis	9	No	..	X	Satisfactory
14	M	12	7	Universalis	5	No	X	..	.....
15	F	28	24	Universalis	4	No	..	X	.....
16	F	25	12	Universalis	4	Yes	Eyelashes only	..	Unsatisfactory

TABLE 2.—*Alopecia Patients Failing to Respond to Cortisone Therapy*

Case	Sex	Age	Age at Onset	Type of Alopecia	Duration of Last Attack, Yr.	Active Disease Throughout Puberty	Duration of Therapy, Weeks	Total Dosage, Gm.
17	F	24	12	Areata	12	Yes	9	4.25
18	F	17	10	Universalis	7	Yes	17+	9.55+
19	M	42	38	Areata	4	No	6	4.65
20	M	16	3	Universalis	13	Yes	10	4.57
21	M	22	8	Totalis	14	Yes	12	9.27
22	M	45	25	Universalis	20	No	11	9.10

TABLE 3.—*Comparison of Alopecia Patients Responding and Not Responding to Therapy*

	Number	Average Age at Onset	Patients with Prepubertal Onset, %	Patients with Active Disease Throughout Puberty, %	Average Duration of Last Attack, Yr.
Patients responding	16	21.4	37	12	4⅝
Patients not responding	6	16.0	66	66	11⅝

ment of old patches of baldness at the same time that hair grew actively in other previously bald areas. This phenomenon was regarded as a sign of very active disease at the time of medication.

The degree of regrowth of hair appeared to be dependent on several factors: firstly, on the dosage of cortisone; secondly, on the duration of the disease, and thirdly, on its severity. The role of the time element was quite conspicuous. Patients with long-standing alopecia were likely to have less regrowth than those with disease of shorter duration. Furthermore, in the same patient, bald patches that had been present for a long time responded less favorably or not at all as compared with bald patches of more recent origin (fig. 1). In all patients but one the regrowing hair was normally pigmented. In this one patient (a 57-year-old woman, patient 2), the growing hair was white, a common occurrence in spontaneous regrowth in all age groups. The texture of the newly growing hair was eventually similar to the hair present prior to the disease. In patients with alopecia areata the new hair blended well with that already present. The new hair was firmly rooted and grew at a physiological rate as long as the cortisone dosage was continued above the critical maintenance level.

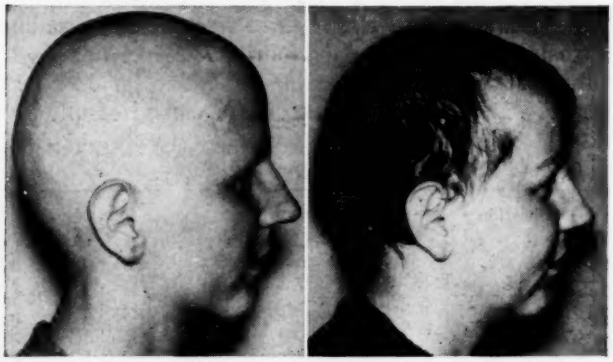

Fig. 1 (patient 15).—Left, alopecia universalis of four years' duration. Right, scalp hair regrowth after four months of therapy with orally administered cortisone. Note persistent patch of baldness at temple and absence of regrowth of eyebrows and eyelashes.

Fig. 2 (patient 4).—Left, alopecia areata of two years' duration. Right, regrowth of hair after 5½ months of therapy.

Seven patients have to date been treated for a sufficiently long period (from 15 to 30 weeks) to permit an evaluation of the result from the cosmetic point of view. After all, this is the most important practical aspect of the treatment of this disease. In four of these seven patients the cosmetic result has been satisfactory (see figure 2). In the other three the growth has been too patchy and sparse to satisfy the requirements of a good appearance, and in these three we do not expect further improvement of the cosmetic results (fig. 3 and 4).

Failures.—Six patients, after 6 to 12 weeks of therapy, failed to show any hair growth or showed growth of only a few hairs. Two patients in this group had universal loss of hair, one had nearly universal alopecia, one total alopecia of the scalp, and two had alopecia areata. Four of these six patients had active disease throughout adolescence (table 2).

A comparison of data of patients who did and did not respond to the administration of cortisone is presented in table 3. There seem to be two significant factors discernible in these data. One is the longer average duration in the cases of failure. In the group of failures the average duration of the last attack had been 11⅔ years, with a maximum duration of 20 years and a minimum duration of 4. In the group that responded to cortisone, the average was 4⅔ years, with a maximum of 14 years and a minimum of three months. A partial explanation for failures in cases of long duration may be found in the fact that after prolonged absence of hair growth the follicular epithelium becomes atrophic and eventually disappears entirely. Another apparently significant finding has been that in the group of failures 4 out of 6 patients had the history of active disease during the adolescent years, whereas only 1 out of 16 of the responding

Fig. 3 (patient 6).—Left, alopecia areata continually present for 14 years. Right, regrowth of scalp hair after six months of therapy.

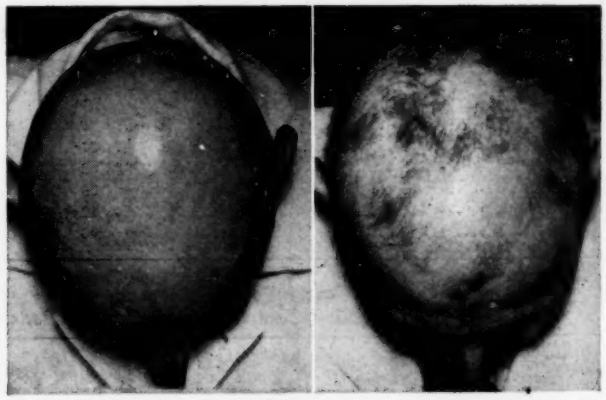

Fig. 4 (patient 12).—Left, alopecia universalis of nine months' duration. Right, patchy regrowth of scalp hair after three months of therapy.

patients had such a history. The poor outlook for patients with a history of pubertal disease may be linked with the previously quoted findings [1] that the course of the disease was much severer when it had its onset before puberty.

Nail Changes.—One patient in our series, in addition to alopecia universalis, also suffered from severe trophic nail changes (fig. 5). This condition responded well to cortisone also. The patient, being an obstetrician, was more concerned with the nail changes than with the hair loss because of the discomfort accompanying scrubbing in the delivery room. These changes have now begun to recur with lowering of the cortisone dose to 25 mg. daily.

Side-Effects.—Fourteen of 22 patients gained weight while under therapy; this, however, was gradually lost as the dose of cortisone was decreased. Hypokalemia developed in two patients, with clinical manifestations of drowsiness and muscle aches. Two patients had acneiform eruptions, which responded well to mild sulfur and resorcin lotions. One patient had menstrual disturbances, another had pitting edema of the ankles, and still another had renal colic on two occasions. The renal colic apparently resulted from crystallization in concentrated urine of uric acid that was being excreted in increased amounts

Fig. 5.—Left, trophic nail changes associated with alopecia universalis. Right, improvement in nails after three months of therapy.

when the patient was subjected to concentration tests. It was effectively prevented by not allowing the patient to undergo further tests requiring withholding of water (resulting in urine concentration) and by lowering the cortisone dosage to reduce the uric acid excretion.

Histological Study.—Biopsies were made from the vertex of the scalp in 7 patients prior to therapy and in 14 untreated patients with alopecia universalis, alopecia totalis, or alopecia areata of long standing. Serial sections from these cases were examined. Pilosebaceous follicles were present, but the hair bulbs, instead of being deep in the subcutis, were found in the mid or deeper corium. Hair bulbs and sheaths were greatly reduced in size and contained only loose keratin, with shafts of compact keratin being entirely absent. The sebaceous glands in many cases showed an increase in size, and these large glands may communicate with the surface through wide keratin-containing funnels (fig. 6). In long-standing cases there was gross thinning of the corium, which may be reduced down to half the normal thickness (fig. 7). Some loose infiltrate with lymphocytes was seen about the hair follicles in a few instances.

In two cases biopsies were done again after cortisone treatment, and a restitution of normal follicles was seen though there was no change in the thinned corium. While the decision as to whether regrowth of hair is likely with treatment depends on clinical considerations, biopsy may add useful information. When hair follicles are greatly reduced in size and have their hair bulbs high in the

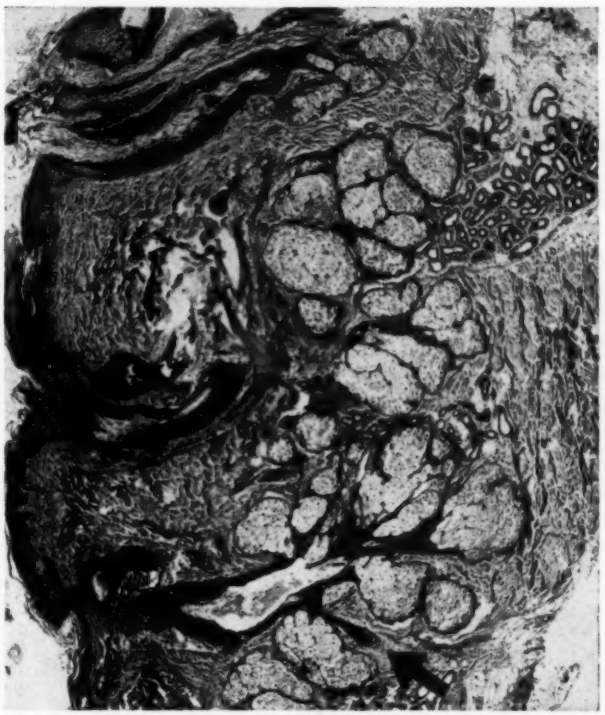

Fig. 6.—Enlarged lobulated sebaceous glands with keratin funnels. Arrow indicates one vestigial hair bulb. (Hemotoxylin and eosin stain, × 37.)

Fig. 7.—There is one small inactive hair follicle, but sebaceous glands are large. There is marked thinning of the corium. (Hemotoxylin and eosin stain, × 49.)

corium (which is thinned), there is unlikely to be any response to treatment, as was the case with the patient whose biopsy is illustrated in figure 6.

COMMENT

There can be no doubt that an adequate dosage of cortisone results in hair growth in alopecia areata, totalis, and universalis. Coincidence with spontaneous regrowth can be ruled out on the basis of the following observations: 1. Hair starts to appear above the skin surface with fair regularity during the fourth week of therapy. 2. Activity of hair growth clearly depends on the dosage, and the effect is lost soon after therapy is discontinued. Growth can be reinduced with reestablishment of therapy 3. Regrowth has occurred in the fourth week of therapy in a number of cases of long-standing alopecia universalis in which spontaneous regrowth can hardly be expected.[1] 4. Similar results have been obtained by administration of corticotropin (ACTH).[3]

The mechanism whereby cortisone stimulates hair growth in this disease is obscure. The causative agent of the disease is unknown. However, it is highly improbable that cortisone acts directly on this agent, otherwise its effect would be less evanescent. Possibly cortisone acts by a change in local chemical milieu through some such manner as influencing sebaceous gland function or keratinization. Although the effect of cortisone in alopecia areata is biologically and pathologically most remarkable and gives some clue for further research on this obscure ailment, the clinical practicality of this type of treatment is highly problematic at the present time. The authors wish to state with great emphasis that they do not recommend this form of therapy for general use.

SUMMARY

Twenty-two patients with severe alopecia areata, mostly of the totalis and universalis types, were treated for 10 weeks or more with orally administered cortisone. There was regrowth of hair in 16 of these patients. In some the hair regrowth, although not complete, was cosmetically satisfactory. However, in the majority of cases the regrowth was patchy. This form of therapy is not recommended for general use.

Waldon Bldg., Little Rock, Ark. (Dr. Dillaha).

3. Wilson, R. A.: Effect of ACTH on Hair Growth in Alopecia Areata and Universalis: Preliminary Communication, Lancet 1:646 (March 29) 1952.

SCIATIC AND FEMORAL NERVE BLOCK

Daniel C. Moore, M.D., Seattle

One of the most useful yet most neglected anesthetic procedures is the combination of sciatic and femoral nerve block. The physician who treats a large number of diabetics or patients with minor or major accidental injuries of the legs will find this block most useful. The technique of a satisfactory sciatic-femoral nerve block is simple to master, and the procedure is almost free of complications, which makes it useful to the general practitioner as well as to the specialist. Sciatic-femoral nerve block has been neglected by most physicians for the following reasons: 1. Spinal (subarachnoid) analgesia is regarded as easier to master and less time consuming to perform, and the results are believed more predictable. 2. Poor results often occur from solely blocking the sciatic nerve for work on the foot. This is because the foot is partly supplied by the femoral nerve (see figure 10, variation). 3. In many training centers these nerve blocks are not adequately taught. 4. Some anesthesiologists comment "that this particular block is little employed and that shock and other circulatory phenomena from trauma to the sciatic nerve occur."[1]

This paper reviews the technique of combined sciatic and femoral nerve block and reports its use in 805 patients (table 1).

TECHNIQUE

The techniques used for blocking the sciatic and femoral nerves are essentially those described by Labat.[2] For sciatic block, the patient is placed in the lateral decubitus position, with the side to be blocked uppermost. The under leg is straight, and the hip joint of the upper leg is in 40 degrees of flexion, 20 to 30 degrees of adduction, and neutral as to rotation. The knee of the extremity to be blocked is flexed at a 90 degree angle (fig. 1 and 2). This position places the nerve on stretch and fixes the anatomic relationship. The posterior iliac spine and superior border of the greater trochanter are located, and the skin overlying these two points is marked. A straight line is drawn between these two points. At the midpoint of this line, another line perpendicular to it is drawn downward. An X mark is made 1½ in. (3.8 cm.) to 2 in.

TABLE 1.—*Use of Sciatic-Femoral Nerve Block in 805 Cases*

Operation	Number of Cases	Maximum Anesthesia Time, Hr.	Maximum Operating Time, Hr.
Closed (reductions, manipulations, Kirschner wires)	295	2	1¼
Open (reductions, tendon repairs, bone grafts, bone resections)	510	5¼	4½

(5 cm.) below the base line (fig. 1 and 2). This point should overlie the sciatic nerve as it emerges from the pelvis by way of the greater sciatic notch. The area is then aseptically prepared and draped.

In administering the anesthetic, the anesthesiologist stands facing the buttocks of the patient. The patient is instructed to say "now" and to avoid movement as soon as he feels a "tingle" or an "electric shock" go down his leg. A skin weal is raised at the predetermined point, and infiltration of the subcutaneous tissues and muscles is performed. A 3 in. (7.6 cm.) or 4 in. (10.2 cm.), 22-gage security Lok needle, depending on the size of the patient, is introduced through the weal perpendicular to the skin in all planes and advanced until paresthesias of

From the Department of Anesthesia, the Mason Clinic.

Read before the Section on Anesthesiology at the 101st Annual Session of the American Medical Association, Chicago, June 10, 1952.

1. Adriani, J.: Techniques and Procedures of Anesthesia, Springfield, Ill., Charles C Thomas, Publisher, 1947.

2. Labat, G.: Regional Anesthesia: Its Technic and Clinical Application, ed. 2, Philadelphia, W. B. Saunders Co., 1928.

the sciatic nerve are elicited. Depending on the size of the buttocks, the depth to which the needle must be inserted may vary from 2 in. (5 cm.) to 4 in. (10.2 cm.). When bone, the rim of the sciatic notch, or the spine of the ischium and the bone in its immediate vicinity are encountered but paresthesias are not obtained, the needle depth should be noted. The needle does not need to be inserted in any direction more than ¾ in. (2 cm.) past this depth. The nerve usually lies more superficial to these parts of the iliac bone, and paresthesias are often obtained before the bone is encountered.

If paresthesias are not elicited, the needle point is withdrawn slightly and reinserted in various directions, in a seeking manner, upward and downward in the plane of the body indicated by the short perpendicular line (fig. 3). If this maneuver fails to produce paresthesias, it should be repeated after the needle has been directed sacrally so as to enter the sciatic notch. When paresthesias are elicited, the motion of the needle is stopped and 15 cc. to 25 cc. of tetracaine (pontocaine®) hydrochloride solution are injected (fig. 4). If, after numerous attempts, no

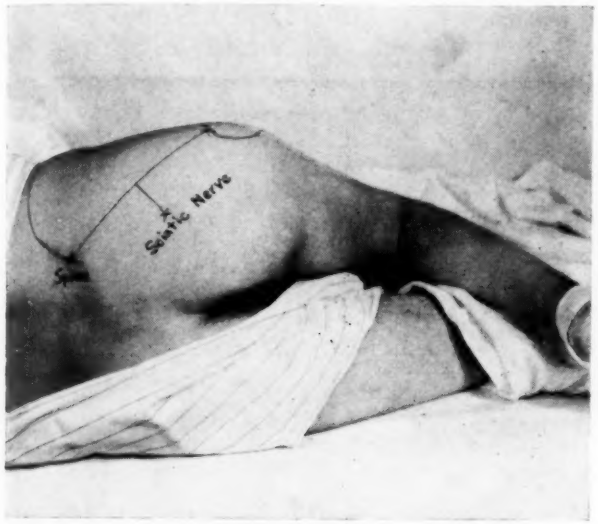

Fig. 1.—Patient in position for sciatic nerve block. Note position of legs and position of X's. Anesthetic administered for fractured ankle. (This and the following illustrations are from Moore, D. C.: Regional Block, Springfield, Ill., Charles C Thomas, Publisher, to be published.)

paresthesias are obtained, 15 to 30 cc. of solution may be injected while the needle point is being moved along the bony rim around the greater sciatic notch in an effort to block the nerve by diffusion of the local anesthetic. The diffusion technique of blocking the sciatic nerve is usually unsatisfactory owing to its large size, and the percentage of partial or complete failures is high.

Following completion of the sciatic nerve block, the patient is turned to the supine position for femoral nerve block, with his hands placed behind his head. The inguinal ligament and the femoral artery are located by palpation. A mark is made on the skin ¾ in. (2 cm.) below the inguinal ligament and just lateral to the femoral artery. This indicates the position of the underlying femoral nerve (fig. 5 and 6). The area is prepared and draped, and a skin weal is raised at the mark. The index finger of the free hand continually palpates and retracts the artery medially while a 1½ in. (3.8 cm.), 22-gage security Lok needle, without the syringe attached, is inserted perpendicular to the skin and advanced until its point lies in close approximation to the lateral side of the artery (fig. 7 and 8). If this vessel is pierced, no concern need be felt, the needle being immediately withdrawn from the lumen of the vessel and redirected slightly laterally. When the operator removes his hand from

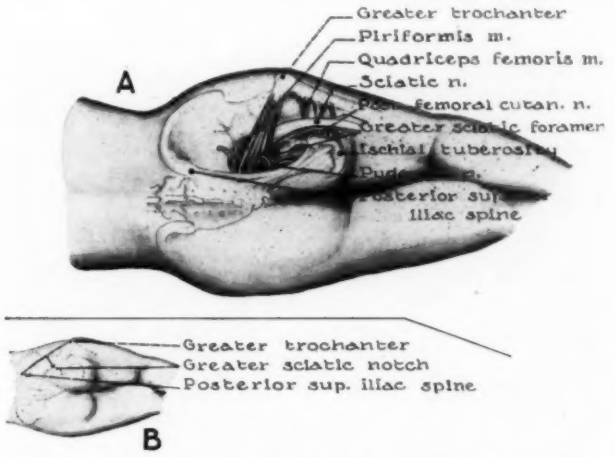

Fig. 2.—*A*, deep anatomy of sciatic nerve in relationship to landmarks. *B*, topographical anatomy of landmarks for sciatic block.

the needle, the needle should oscillate in rhythm with the adjacent femoral pulse. Twenty cubic centimeters of anesthetic solution is now injected in a fanwise plane lateral to the artery, the injection being carried out as the needle is moved in and out (fig. 9). Care should be taken to see that a wall of anesthetic solution is deposited from the skin to a depth of 1¼ in. (3.2 cm.) and laterally from the artery a distance of at least 1 in. (2.5 cm.). This fanwise injection should be distributed along a cross sectional plane of the upper thigh. No attempt at eliciting paresthesias is made for the femoral nerve, for the diffusion technique of blocking the femoral nerve is, in contrast to the sciatic, close to 100% successful.

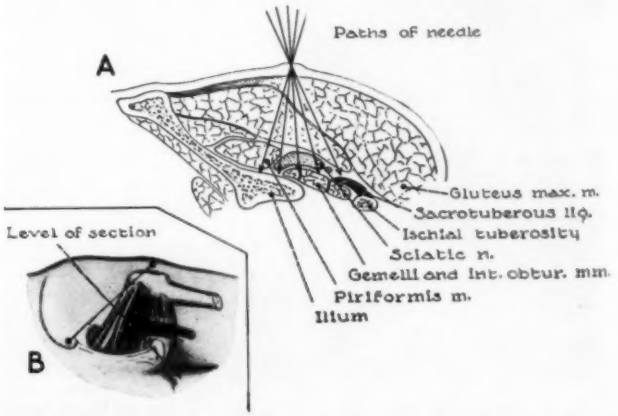

Fig. 3.—*A*, direction in which needle should be readjusted when seeking paresthesias of sciatic nerve. *B*, level of section.

Should paresthesias occur, however, 5 cc. of solution is injected at that point.

Tetracaine hydrochloride has been the anesthetic drug of choice (table 2). Concentrations of 0.15 to 0.25% and volumes ranging from 30 to 100 cc. have been employed. It is best never to exceed 1 mg. of tetracaine per pound of body weight. When a bilateral sciatic-femoral

block is performed, the weaker solutions should be employed. Epinephrine (adrenalin®), 0.2 cc., and hyaluronidase, 150 turbidity reducing units, may be incorporated in the solution. If hyaluronidase is used, epinephrine should be added to the solution or the anesthesia time will be markedly shortened due to wider diffusion and quicker absorption of the drug.

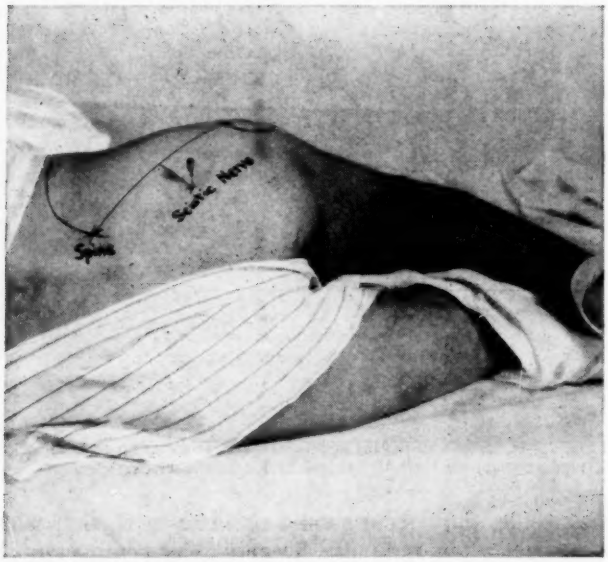

Fig. 4.—A 3 in. (7.6 cm.) needle in place for sciatic block. Paresthesias were just elicited. Note perpendicular position of needle.

Fig. 5.—Landmarks and position of patient for femoral nerve block: A.S.S., anterior superior spine of iliac bone; L.F.C., lateral femoral cutaneous nerve; F.N., femoral nerve; P.S.; pubic spine; O.N., obturator nerve.

RESULTS

Combined sciatic-femoral nerve block was used in 805 cases, 490 by myself and 310 by J. J. Bonica and resident staff.[3] A wide variety of operations on the leg from 2 in. (5 cm.) below the knee was performed (see table 1). Anesthesia was completely satisfactory in 9 out of 10 cases and required no supplementary anesthesia whatsoever. From the anesthetic standpoint, it is felt that a block should be either considered completely satisfactory in itself or judged unsatisfactory. This classification allows no category for a partially successful block. Despite this strict rule, 90% of the blocks were completely satisfactory, the instructor's percentage being slightly higher than the residents'. All persons in this series were private patients, a fact that supports my belief that this combination of blocks is highly satisfactory from the patients' standpoint; for otherwise, by demand, its use would be limited to the exceptional instance rather than prescribed for the routine cases. The blocks were performed on patients ranging from 10 to 90 years of age and of varying physical status. Outpatients, emergency patients, and diabetics comprised approximately 25% of the cases.

There were no serious complications from the block technique and only two minimal reactions (0.25% of

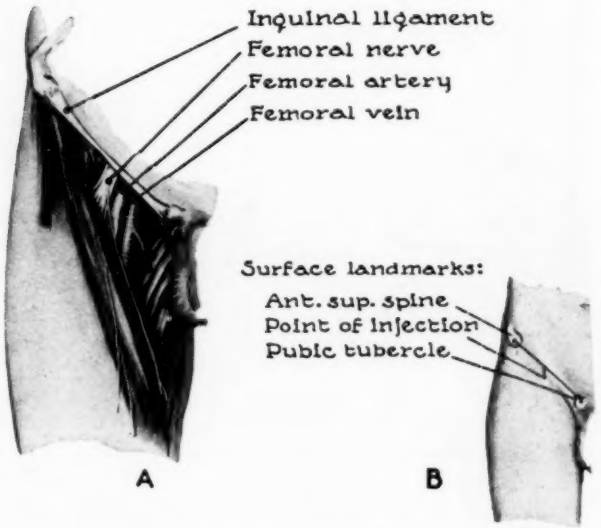

Fig. 6.—Area involved in blocking of femoral nerve: *A*, deep anatomy; *B*, topographical anatomy.

805 cases) to the local anesthetic agent and/or the vasoconstrictor agent. In both of these cases, 50 cc. of the stronger concentration, namely, 0.25% tetracaine hydrochloride with 0.2 cc. of epinephrine, was used. One reaction occurred in an 18-year-old woman undergoing arthrodesis of the ankle and was characterized by an irregular pulse that reverted to a normal rhythm in 10 minutes without any treatment. The other reaction occurred in a 48-year-old man who had a closed reduction of the ankle and was characterized by blood pressure fall, sweating, pallor, and faintness. Ephedrine sulfate (25 mg.) intravenously and oxygen inhalation corrected the condition in five minutes.

Surgical analgesia from the combination of these two blocks extends throughout the leg and foot to about 2 in. below the patella. Skin analgesia over part of the in. (5 cm.) below the patella. Skin analgesia over part of the medial, posterior, and a small portion of the lateral surface of the thigh ensues (see figure 10). Closed man-

3. Bonica, J. J.: Personal communication to the author.

ipulations of the thigh may be done, but open operations cannot be performed unless the obturator and lateral femoral cutaneous nerves are also blocked, since they supply much of the skin of the thigh. It must be remembered that I strive to start all block anesthetic procedures at least 45 minutes before surgery in order to give adequate time both for instruction and for the block to become established. Also, I do not hesitate to do a nerve block again if my first attempt is a failure or if only partial anesthesia is obtained.

COMMENT

Paresthesias of the sciatic nerve should be elicited to assure a satisfactory block of that nerve. Paresthesias of the sciatic nerve that are characterized by a "shooting, electric-like" pain to some portion of the foot should not be confused with the sensation derived from stimulation of the iliac periosteum, which often radiates into the thigh as a dull, aching pain. My dictum for this block is "No

Fig. 7.—Index finger displacing femoral artery medially as femoral nerve is injected. Parethesias were not elicited in this patient, but pulsation of the artery against needle was easily felt. A satisfactory block ensued.

paresthesias, no anesthesia." Because paresthesias are essential, the patient should be awake and cooperative at the time the block is performed. For this reason, premedication is gaged and selected when the patient is seen on preoperative rounds.

Premedication in the average patient, who, for example, is 20 to 50 years of age, is 5 ft. 10 in. (177.8 cm.) tall, weighs 150 lb. (68 kg.) or over, and is in good physical condition, consists of ⅙ grain (10 mg.) to ¼ grain (15 mg.) of morphine sulfate with 1/150 grain (0.4 mg.) to 1/100 grain (0.6 mg.) of scopolamine or atropine at the time of call to surgery. A barbiturate is not given preoperatively. Prior to the injection of the blocking drug into the femoral nerve 1½ grain (90 mg.) to 3 grains (180 mg.) of pentobarbital (nembutal®) is given intravenously. The patient thus seldom remembers the femoral block or is discomforted by it. If the patient is restless prior to or during the surgical procedure or misinterprets touch as pain, he is given additional sedation, usually intravenously, such as morphine, meperidine (demerol®) hydrochloride, pentobarbital, or 0.2% thio-

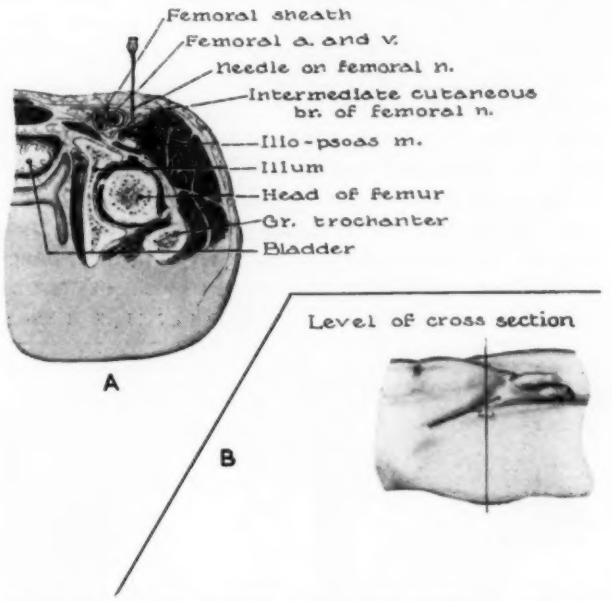

Fig. 8.—*A*, anatomy of femoral nerve at level of injection, with needle lying next to artery in vicinity of nerve. *B*, level of cross section.

pental (pentothal®) sodium. I always bear in mind Labat's admonition that, "Narcotics must be used to blunt consciousness but not to abolish it." [2]

TABLE 2.—*Effectiveness of Tetracaine (Pontocaine®) Hydrochloride in Sciatic-Femoral Nerve Block*

Number of Cases	Drug Concentration, %	Drug Volume, Cc.	Onset Time of Analgesia, Min.	Amount of Vasopressor, Cc.	Duration, Hr.
332	0.15	30 to 90	20 to 30	0.2	4 to 6½
473	0.25	40 to 50	10 to 15	0.2	4 to 6½

For the past five years tetracaine hydrochloride has been my choice for the local anesthetic agent. I prefer the crystalline form and mix my own solution; however,

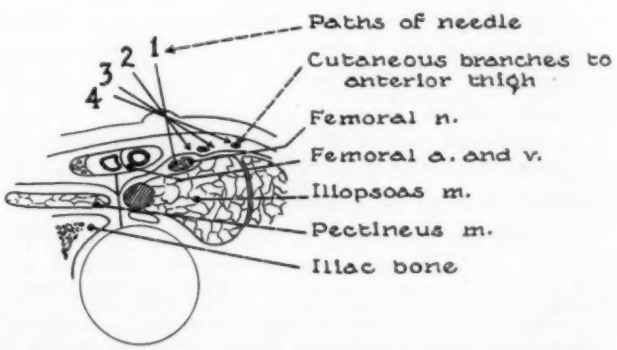

Fig. 9.—Cross section through thigh showing lateral fanwise direction of needle as femoral nerve is injected. Cross section is through same area shown in figure 8.

ready-mixed tetracaine solutions are adequate.[3] In the effective concentrations advocated here, it is no more toxic than procaine (novocaine®) hydrochloride and in

many instances is less toxic.[4] Not more than 1 mg. of tetracaine per pound of body weight is administered, and as a result its toxic reactions are relatively infrequent in comparison with those of procaine and are treated in the same manner. Again, I prefer tetracaine inasmuch as it produces an anesthesia that lasts four to six hours, with solutions containing epinephrine giving longer durations (see table 2). There are several advantages based on this lengthy duration. First, the anesthesiologist has time to do the block deliberately without rushing, there is adequate time to instruct pupils, and lengthy dissections may be performed under local anesthesia. Second, sudden changes in operating schedules are permissible, since the nerve block does not have to be done again even if the operation is delayed up to two or three hours. Third, the anesthesiologist has some convenient personal latitude as to timing his blocks, which is of obvious

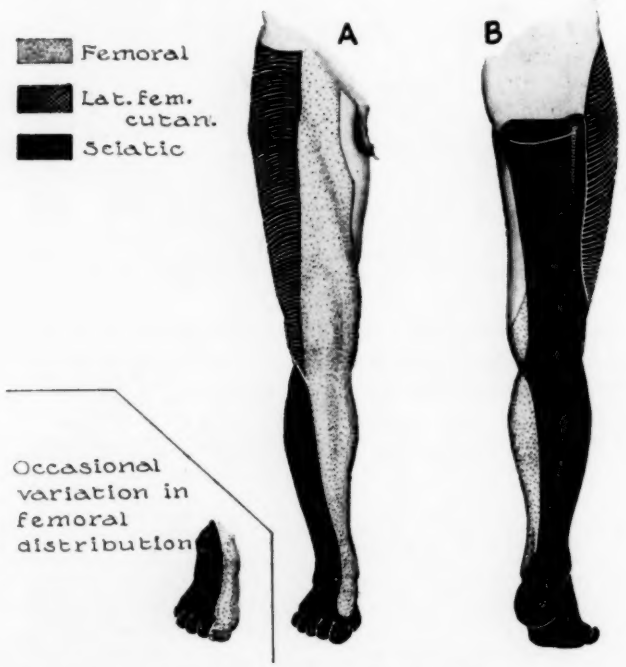

Fig. 10.—Area of skin anesthesia resulting from block of sciatic nerve and femoral nerve: *A*, anterior and *B*, posterior views.

importance in private practice where a large surgical schedule is the rule. Last, the length of anesthesia and postoperative analgesia reduces the amount of postoperative opiates.

It was found that by strict adherence to the technique described herein that in a short period of time the residents' percentage of successful blocks closely paralleled those of the instructor. This point is emphasized because many physicians believe the combination of sciatic and femoral block is difficult, time consuming, and unsatisfactory in a high percentage of cases. I wish to rectify these impressions and to stress that with patience and some basic understanding of anatomy these blocks can be mastered by most physicians. While it is true that spinal analgesia will create the same operating conditions as sciatic and femoral block and that the spinal technique may be easier to master, there are certain drawbacks to spinal analgesia that have caused me to prefer the combination of sciatic and femoral block wherever it is applicable. 1. Following spinal analgesia the patient is nonambulatory. This should be considered when a patient is treated on an outpatient status, or during war or catastrophe when it may be necessary to move patients quickly. Following combined sciatic-femoral nerve block, patients may be ambulatory on crutches almost immediately. 2. Sciatic and femoral nerve block circumvents the 7 to 10% incidence of headache that occurs after spinal analgesia. 3. Most patients who complain at the prospect of a contemplated spinal anesthetic will not object to a sciatic-femoral nerve block. 4. Other dangers associated with spinal anesthesia, such as precipitous fall in blood pressure, nausea, vomiting, high anesthesia, and caudo-equina syndrome, are avoided.

Combined sciatic and femoral nerve block offers certain advantages to the patient and physician that are not usually possible with general anesthesia. 1. The chemical sectioning of the nerve allows conservation of the physiological economy of the patient, which is of obvious importance in cardiac disease and diabetes. 2. Emergency procedures may be done immediately without the hazard of vomiting and aspiration even after a full meal. When fluoroscopy is necessitated, this block eliminates respiratory depression or obstruction that may go unnoticed in a dark room. 3. Postoperative nausea, vomiting, and atelectasis usually do not occur, and postoperative depression that may follow a prolonged general anesthetic is avoided. 4. This block reduces the time needed for postanesthetic care, and the nursing staff may direct more attention to the care of the extremity. 5. In circumstances where it is necessary to limit the amount of time an anesthesiologist must spend with each patient (for example, the treatment of lower extremity injuries under catastrophic conditions), this type of block is less time consuming and more practical than general anesthesia.

SUMMARY AND CONCLUSIONS

An effective technique for combined sciatic and femoral nerve block that has given 90% satisfactory blocks out of 805 cases is described. The advantages of this combined block are enumerated and compared with spinal and general anesthesia. The reasons why tetracaine (pontocaine®) is the drug of choice are discussed. The results obtained in this series of cases justify a belief that this block combination is an entirely satisfactory form of anesthesia for operations and manipulations of any part of the leg and foot from 2 in. (5 cm.) below the patella down. Perseverance, a knowledge of the anatomy involved, and strict observance of the principles of the technique described will permit most physicians to master this technique and to obtain satisfactory results.

1115 Terry Ave.

4. Novak, S., quoted by Saklad, M.: Spinal Anesthesia: Agents, Methods and Indications, New England J. Med. **213**: 1226 (Dec. 19) 1935. Moore, D. C.: Pontocaine Hydrochloride for Brachial Block Analgesia: 150 Cases, Anesthesiology **9**: 218 (May) 1948; The Use of Pontocaine Hydrochloride for Nerve Block and Infiltration Analgesia, Therapeutic and Diagnostic Blocks: 1,004 Cases, ibid. **11**: 65 (Jan.) 1950. Moore, D. C., and Bonica, J. J.: Combined Brachial Block and Spinal Analgesia for Bone Graft Surgery (Report of 83 Cases), Anesth. & Analg. **29**: 43 (Jan.-Feb.) 1950. Bonica, J. J.; Moore, D. C., and Orlov, M.: Brachial Plexus Block Anesthesia, Am. J. Surg. **78**: 65 (July) 1949. Moore, D. C.: Pontocaine Solutions for Regional Analgesia Other than Spinal and Epidural Block, J. A. M. A. **146**: 803 (June 30) 1951. Bonica, J. J.: Regional Anesthesia with Tetracaine, Anesthesiology **11**: 606 (Sept.) 1950.

MYCOTIC ANEURYSM OF THE CIRCLE OF WILLIS

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and
Johannes F. Pessel, M.D., Trenton, N. J.

In the Gulstonian Lectures of 1885, Sir William Osler [1] stated, "The meningeal complication of endocarditis has not received much attention." Osler's remark is as revealing today as it was then.

We shall review a case of subacute bacterial endocarditis in which a mycotic aneurysm of the right middle cerebral artery was discovered at autopsy. This lesion of the intracranial vessels has been noted in only 34 previous cases.[2] A brief review of the pathological changes of mycotic aneurysm of the circle of Willis will be given. In the present period of antibiotic therapy, studying a case of this type constitutes a rare pathological experience.

REPORT OF A CASE

An unmarried white woman, 50, was admitted in a comatose condition with a left hemiplegia of six days' duration. She was known to have recently had a blood transfusion and to have had severe anemia for over two years. Liver extract had been given for the anemia. The family stated that she had always been weak. She had undergone a hysterectomy two years previously for uterine tumors.

Examination disclosed relative cardiac dulness in the left midaxillary line with the point of maximal impulse in the left anterior axillary line at the sixth interspace. A loud blowing systolic bruit was best heard over the apex of the heart and was well transmitted to the left posterior portion of the chest. Blood pressure was 126/74, pulse rate 96, and temperature 100.6 F. Fist percussion over the kidney area was painful.

The urine was positive for occult blood, with 65 mg. albumin and a rare granular cast. Hypochromic anemia was verified, with 7 gm. of hemoglobin and 2,500,000 red blood cells. The blood urea nitrogen was 80 mg. with a total protein of 7 gm. The blood was a type A, Rh positive, and Hr′ positive; serologic reactions were negative.

Fig. 1.—Mycotic aneurysms of the right middle cerebral artery, indicated by the arrow. The white granular necrotic wall is characteristic of the gross lesion. Thickening of the adjacent segments of the middle cerebral artery due to acute arteritis is shown, as well as pressure necrosis and hemorrhage involving the adjacent cerebral tissue.

While in the hospital, the patient had a septic temperature, varying from 98 to 102.8 F. Her comatose condition changed to semistupor after a blood transfusion and penicillin therapy. However, she was unable to speak at any time and died on the fifth day of hospitalization.

Autopsy revealed an enlarged heart, weighing 410 gm., and left ventricular hypertrophy with a partly calcified, crayfish-like vegetation, measuring 1.4 by 0.6 cm., attached to the free edge of the posterior mitral leaflet. The spleen weighed 350 gm. and showed gross infarction. Both kidneys were enlarged, weighing 210 gm., and showed a light pink-gray cortical surface with numerous pinhead petechial hemorrhages having a spider-like outline when the capsule was removed. Histological study confirmed the presence of focal endocarditic glomerulonephritis.

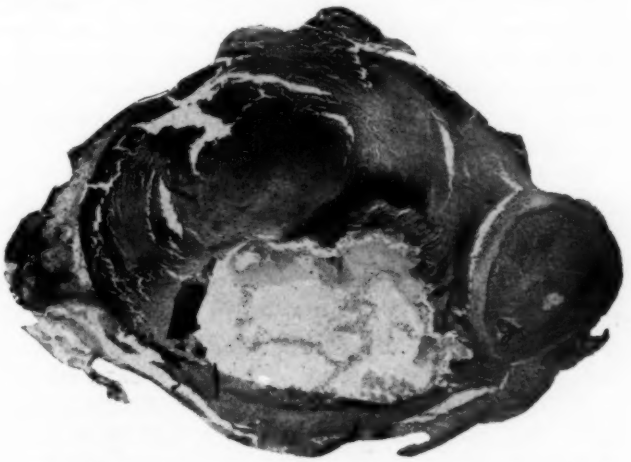

Fig. 2.—Photomicrograph of the area of acute arteritis, with practically complete destruction of the internal elastic lamina of the right middle cerebral artery incident to the lodgement of an infected embolus and production of a mycotic aneurysm.

The brain weighed 1,400 gm. and showed a mycotic aneurysm, with a diameter of 0.7 cm., of the right middle cerebral artery. The sac arose at a point 1 cm. beyond the junction of the right posterior cerebral and right anterior cerebral arteries with the right internal carotid artery (fig. 1). A conspicuous feature of the aneurysmal sac was a gray-white wall of granular necrotic tissue. The associated subarachnoid hemorrhage and regional necrosis involved the anterior limb of the right internal capsule and a part of the right caudate nucleus of the basal ganglions.

Microscopic study of the aneurysmal sac disclosed a fibrohyaline-like mass lodged within the vascular lumen, with necrosis of the adjacent intima and destruction of the internal elastic lamina at this point, the area of lodgement being the site of an acute polymorphonuclear exudate of mesarteritis and periarteritis (fig. 2). The periarteritis and mesarteritis extended for an appreciable distance along the wall of adjacent small arteries. Gram stain of the aneurysmal sac showed numerous gram-negative diplococci, morphologically similar to pneumococci, and which we categorized, on a morphological basis, as Friedländer's pneumobacillus.

COMMENT

Because of the absence of conclusive bacteriologic proof, one may question the diagnosis of subacute bacterial endocarditis in this case on an empirical basis; however, the demonstrated anatomic lesions plus the microscopic myocardial lesions of subacute bacterial endocarditis, when evaluated with the reported history, fully justify this diagnosis.

From the departments of pathology and medicine, Mercer Hospital.

1. Osler, W.: The Gulstonian Lectures on Malignant Endocarditis, Brit. M. J. **1**: 467-470, 1885.

2. Stengel, A., and Wolferth, C. C.: Mycotic (Bacterial) Aneurysms of Intravescular Origin, Arch. Int. Med. **31**: 527-554 (April) 1923.

The mycotic aneurysm of the right middle cerebral artery constitutes a rare lesion of the circle of Willis, the congenital or berry aneurysm being a more frequently encountered entity. We have never noted the wall of a berry aneurysm to show white granular necrosis in a section of the gross specimen.

Sir William Osler adopted the term "mycotic" for aneurysms of this type. Virchow in 1847 furnished proof that embolism occurs and noted that at the seat of the embolism destruction of the inner and middle arterial coats may be found. Unger showed that, when emboli plug the lumen of an artery, inflammatory processes begin on the inner surface and spread outward. Eppinger demonstrated that the infection was conveyed by bacteria-laden emboli detached from the heart valves to the arterial wall and that formation of an aneurysm was dependent on partial disintegration of the wall, particularly the internal elastic lamina.

MacCallum [3] divided mycotic aneurysms into four classes: 1. Those plainly due to extension of infection from an embolus lodged in the arterial lumen. The aneurysm in our case belongs in this class. 2. Implantation aneurysms, in which bacteria are implanted from flapping fragments of an infected valve. 3. Those of obscure origin, either due to accidental lodgement of bacteria on the intima or resulting from embolism of the vasa vasorum. 4. Mycotic aneurysm from external erosion of the vessel wall due to extension of infection from an external focus.

The middle cerebral artery is the most frequent site for mycotic aneurysm. Most patients are seen in the second, third, or fourth decades of life. Syphilitic aneurysms of the systemic vessels occur most often in the fifth decade.

The most characteristic findings are loss of the intima, destruction of the elastic tissues (particularly the internal elastic lamina), and acute or subacute periarteritis and mesarteritis. In the more acute conditions, micro-organisms are often found in enormous masses, and there may be a severe reaction of polymorphonuclear leukocytes.

Stengel and Wolferth [2] stated that intracranial mycotic aneurysms have not been diagnosed clinically. In many cases, no symptoms were discovered that could be related to the aneurysm found at necropsy. Clinical signs, when present, have been merely those of embolism, intracranial hemorrhage, or both.

This patient's hemiplegia, which occurred six days prior to hospitalization, was, in our opinion, directly due to the necrosis of the anterior limb of the internal capsule, incident to rupture of the mycotic aneurysm. The aneurysm developed after lodgement of an infected embolus from a vegetative endocarditis of the mitral leaflet. The endocarditis presumably had been present for some time and contributed in no small way to the patient's manifest anemia. This anemia will not respond to treatment with liver extract. Despite the widespread use of antibiotics, patients who are examined post mortem may still show mycotic aneurysms of intravascular origin, just as they did in the era of Osler. Some evidence exists that the endocarditis was due to an infection by Friedländer's pneumobacillus.

CONCLUSIONS

1. Postmortem study of a patient with anemia of unknown cause showed her to have anatomic lesions of subacute bacterial endocarditis and a mycotic aneurysm of the circle of Willis.

2. History and pathological changes of mycotic aneurysms are reviewed.

3. In anemia, the diagnosis should always precede therapy.

446 Bellevue Ave. (8) (Dr. Rathmell).

3. MacCallum, W. G.: Mycotic Aneurysms, Tr. Coll. Physicians 51: 6-20, 1929.

METASTATIC CARCINOMA OF THE UMBILICUS

Alfred B. Clements, M.D., New York

Carcinomatous infiltration of the umbilical region has received very little attention in the literature, and a reader on the subject gets the impression that such an occurrence is quite rare. Within a relatively short period of time, however, I have observed four histologically proved cases of umbilical metastases in the medical wards of the Bronx Hospital. Since the umbilical area lends itself readily to biopsic study, the diagnosis of a malignant growth elsewhere may thus be made in otherwise obscure cases; furthermore, the finding of a metastatic nodule at the umbilical site almost certainly establishes the inoperability of the patient. It is the purpose of this report to emphasize the value of careful palpation of the umbilical region, especially when carcinoma is suspected.

From the Department of Internal Medicine, the Bronx Hospital.

Dr. Harry Wessler, Director of the Department of Internal Medicine, the Bronx Hospital, assisted in the preparation of this report; Drs. Abner Stern and Max Weiss furnished the case reports, and Dr. Joseph W. Tandatnick supplied the photomicrographs.

REPORT OF CASES

CASE 1.—A 63-year-old white woman was admitted to the medical service of Dr. Abner Stern with the chief complaints of weight loss and anorexia of three to four months' duration. She also complained of food sticking in her epigastrium after eating. There was no nausea or vomiting, abdominal pains, diarrhea, or melena. She had lost approximately 30 lb. (13.6 kg.), and intermittent hiccups had developed in the two to three weeks prior to her admission. Her history also revealed that a subtotal thyroidectomy had been done four years previously.

Physical examination on admission revealed a thin, chronically ill white woman, with evidence of pronounced weight loss and generalized pallor. The tongue was not smooth. The heart and lungs were normal. The abdomen was soft, but a hard, irregular, nodular mass about 3 cm. in diameter was felt surrounding the umbilicus. The remainder of the physical examination was normal. A test meal showed no free acid in the gastric contents, even after the injection of histamine. A moderately severe hypochromic anemia was present. The stools were negative for occult blood. All other laboratory tests were within normal limits.

A gastrointestinal series revealed that the superior portion of the stomach, extending from the fundus to the antral area, was

replaced by a narrowed, straightened, tube-like structure with secondary deformity. The second duodenal segment was dilated, and the distal portion of the third duodenal segment was visualized poorly. The findings were reported as an advanced malignant growth of the stomach, with involvement of the third duodenal segment and the midtransverse colon.

A biopsy of the umbilical nodule was done under local anesthesia, and a histological examination of the tissue revealed a highly anaplastic carcinoma (fig. 1). A sternal bone marrow puncture showed a normal differential, but, in addition, clumps of large anaplastic tumor cells were occasionally found. The patient became completely anorexic, with hiccups and progressive weight loss. She was given supportive therapy, but she declined rapidly and expired five weeks after admission. Permission for autopsy was not obtained. The final diagnosis was advanced, inoperable carcinoma of the stomach, with metastasis to the umbilicus and the sternal marrow. This very definite diagnosis was established in this patient by the biopsy and examination of the umbilical nodule.

CASE 2.—A 43-year-old white man was admitted to the medical service of Dr. Max Weiss with the chief complaint of insomnia, which he attributed to business problems of the previous two years. These problems had caused him to drink a considerable amount of alcohol, and there was also a history of a suicidal attempt. In spite of all this, however, the patient stated that his food intake had been quite adequate, although there had been a 30 lb. (13.6 kg.) weight loss in the previous year. The patient also complained that he had had a dull pain in the left side of his abdomen for the past few months.

The physical examination on admission revealed the man to be cachectic. The skin had poor elasticity, and there was evidence of weight loss. Examination of the eyes showed an early arcus senilis, exophthalmus, and widely dilated pupils. The heart examination did not disclose any abnormality. On auscultation, diminished breath sounds were heard at both bases of the lungs. The abdomen was tense, and a firm umbilical mass was felt. Ascites was present. Laboratory studies showed normal blood values. The urine was essentially normal except for the presence of bile and urobilinogen, the latter being positive in a dilution of 1 to 50. The values for serum protein and albumin-globulin fractionation were normal, as were other hepatic functional tests. On one occasion occult blood was present in the stool. The gastric analysis was within normal limits, and the sigmoidoscopic examination was normal. Repeated determinations of blood nonprotein nitrogen revealed an increasing azotemia, the last reported value being 61.5 mg. per 100 cc. The x-ray examination of the gastrointestinal tract was suggestive of a lesion on the lesser curvature. A gallbladder series was normal. The examination of the colon by means of a barium enema revealed, in the midascending colon, a pressure defect that seemed to be connected with the liver.

An abdominal paracentesis was performed and the fluid examined for malignant cells, but a definite diagnosis could not be made. On the 13th hospital day the patient complained of severe pain that originated in the left upper quadrant of his abdomen, and radiated across to the epigastrium. The pain was accompanied by vomiting. On examination a voluntary rigidity and diffuse tenderness were elicited, being maximal in the right upper quadrant. A flat x-ray film of the abdomen was taken in order to determine the possibility of a ruptured viscus, but no air could be demonstrated under the diaphragm. In spite of supportive therapy the patient's condition deteriorated progressively and he died on the 21st hospital day.

At autopsy the peritoneal cavity was found to contain about 1,500 cc. of a yellowish, transparent fluid lying in pockets between a shaggy, grayish exudate and a yellowish, gelatinous material that enmeshed the loops of the small bowel, adhering them to each other. An abscess containing about 100 cc. of cloudy, greenish-yellow pus was found between the left lobe of the liver and the stomach. In the region of the umbilicus considerable neoplastic infiltration was present, forming a mass that was palpable externally. In addition, numerous peritoneal implants, both white and hemorrhagic, were present. Careful search of the gastrointestinal tract failed to reveal any evidence of an intrinsic lesion. Large, firm nodes were felt around the neck of the gallbladder and the cystic duct, causing biliary obstruction. There was microscopic evidence of metastatic involvement of the liver. An area of neoplastic infiltration about the left adrenal gland was firm, pinkish-white in color, and measured 2 cm. in diameter. Also, midway down the course of the right ureter was an area of infiltration measuring 1 cm. in diameter; however, no definite primary lesion could be demonstrated. In summation, this patient had an anaplastic adenocarcinoma with diffuse intra-abdominal involvement. Although the site of the primary lesion could not be established, the histological picture suggested it was intestinal rather than gastric. The umbilical nodule was the only clue during life to the existence of an underlying malignant growth. Its finding established the diagnosis.

CASE 3.—A 53-year-old white woman was admitted to the medical service of Dr. Max Weiss with the history of tiring easily, weight loss, abdominal and back pain, and anorexia of several months' duration. Diabetes mellitus had been discovered five months previously, at which time the patient had been placed on insulin therapy. The diabetic control was difficult because of anorexia.

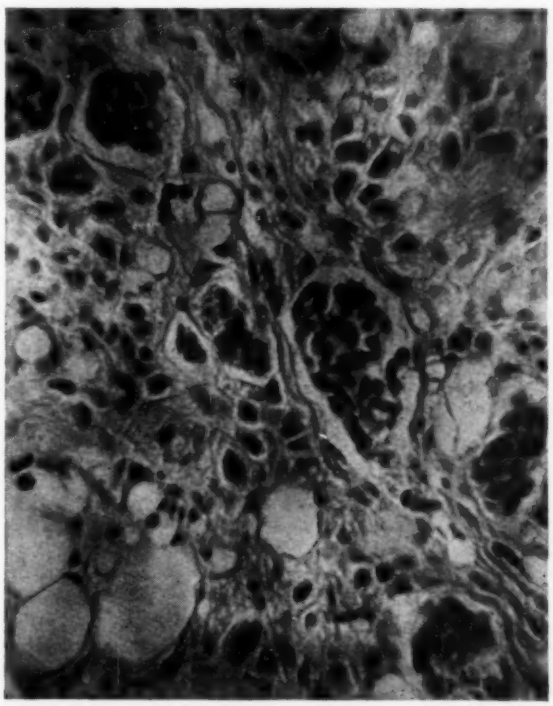

Fig. 1 (case 1).—Section taken from umbilicus, showing small, compact nests of anaplastic carcinoma imbedded in a rather loose connective tissue stroma. The cells are pleomorphic and vary considerably in size. Note penetration of connective tissue by individual tumor cells.

Physical examination revealed an epigastric mass and a small, hard umbilical nodule. The diagnosis of an intra-abdominal malignant growth was made, and an exploratory laparotomy was performed. The entire peritoneum and abdominal viscera were found to be studded by small tumor nodules. The body and tail of the pancreas were enlarged, forming a hard, nodular, fixed mass. A biopsy of a peritoneal metastasis was taken. The pathological report was metastatic adenocarcinoma. The patient had an uneventful postoperative course and was discharged, after eight days, with the diagnosis of carcinoma of the pancreas; however, she became progressively weaker and was readmitted in about six weeks. An abdominal paracentesis was done, and 3,500 cc. of a serosanguinous fluid was removed. The patient's condition remained poor, and she expired three hours later.

At autopsy the peritoneal cavity still contained about 500 cc. of fluid. Numerous peritoneal and omental metastases were noted. Some of these were confluent; others were solitary. Grossly, they were yellowish-white in color and somewhat hemorrhagic. A subcutaneous tumor nodule, which measured 2

by 3 cm., was palpable just above the umbilicus and was continuous with the peritoneal implants. The entire pancreas was replaced by tumor tissue that was firm and adherent to the greater curvature of the stomach. There were numerous nodules in the liver, the largest measuring 2 cm. The pelvic organs were matted together by similar tumor nodules. The gross diagnosis was carcinoma of the pancreas with generalized metastases, but careful study of the microscopic sections revealed that the primary lesion was a pseudomucinous cystadenocarcinoma that originated in one of the ovaries.

CASE 4.—A 76-year-old woman was admitted to the medical service of Dr. Max Weiss with the chief complaints of progressive weakness and a swelling of the abdomen of four months' duration. At the same time urinary frequency developed. She became progressively weaker, which finally necessitated her confinement to bed.

Physical examination on admission revealed a well-developed, pale, weak white woman with a markedly protuberant abdomen. In the neck was felt a firm, fixed node in the left posterior cervical chain, and also palpated were enlarged right posterior cervical and right supraclavicular nodes. The lungs gave off bilateral basal rales. The heart, apparently not enlarged, was in regular sinus rhythm, with occasional premature ventricular contractions. A soft, grade 1 systolic murmur was heard at its apex.

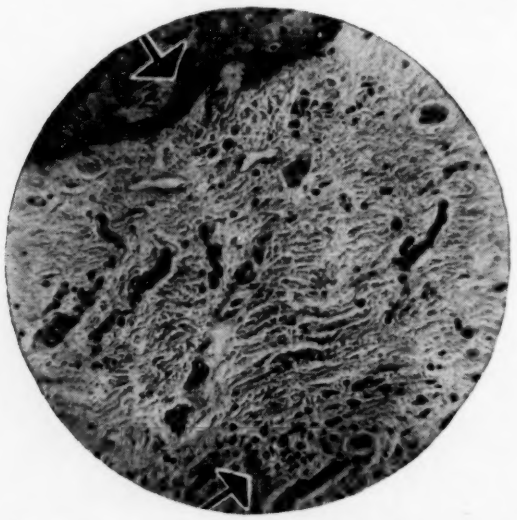

Fig. 2 (case 4).—Section taken from umbilicus, showing normal epidermis (upper arrow), beneath which the subcutis reveals a rather sparse infiltration by individual tumor cells that have the general morphological characteristics of epithelial cells, i. e., carcinoma (lower arrow). The intervening portions of subcutis show numerous small blood vessels and a somewhat hyalinized connective tissue.

The abdominal examination revealed a pronounced ascites, which prevented the palpation of any masses. The rectopelvic examination showed the pelvic organs were fixed, and a mass felt in the rectum was interpreted as a Blumer's shelf. Slight pretibial and ankle edema was present. Radiographic examination showed diffuse, combined metastatic lesions involving the pelvis and upper aspect of the femur. The lytic changes in the sacrum were very evident, and a roentgenogram of the shoulder joints revealed a mottled appearance.

A paracentesis was done, with the removal of 9,000 cc. of fluid. After this the abdominal examination showed that the liver was enlarged to three fingerbreadths below the right costal margin and also that multiple firm, fixed masses were ballotable through the remaining ascites. One of these, located in the umbilical area, measured about 2 cm. in its largest diameter. A biopsy of it was done under local anesthesia, and its examination revealed an undifferentiated, metastatic carcinoma (fig. 2). A biopsy and examination of the lymph node from the left cervical chain presented a similar finding. The primary site of the carcinoma was not determined; but because the finding of the metastatic lesions in the umbilicus and cervical nodes established its inoperability, no further investigations were considered advisable, and the patient was discharged.

COMMENT

In spite of its easy accessibility, the umbilicus remains an infrequently examined area. After a fairly careful search of the literature, the author has found very few references to its involvement by a malignant process. In fact it is surprising that no mention is made of it in the specialized books on neoplastic diseases that were consulted. Even Ewing,[1] whose work in the field of tumor pathology is monumental, does not discuss this subject in his textbook. The only references are those to be found in clinical reports.

Attention was first drawn to the umbilical region in 1916 by Cullen,[2] who reviewed the literature up to that date and compiled 27 cases of umbilical cancer secondary to primary disease in the stomach. In 1945 Lombardi and Parsons [3] collected all other cases mentioned in the literature, bringing the total up to 37, to which they added another of their own. They very emphatically stressed the point that such cases are not rare and recommended that the umbilical region be palpated carefully whenever gastric carcinoma is suspected. The author wishes to emphasize further that the primary site need not be gastric but that other foci may be, and often are, present. In the present series of four cases, two were definitely not gastric in origin, and the primary site in the third case was not established. Williams [4] reported two cases. In one the primary lesion was in the small intestine, and in the other it arose in the left kidney. Rochet and Francillon [5] reported a case in which the primary lesion originated in the biliary tract.

Whenever the umbilical region is involved as part of a generalized carcinomatous invasion of the peritoneal cavity, it may be thought that the finding of an umbilical lesion is merely of academic interest, since in such cases the diagnosis of widespread and inoperable cancer is easily reached; however, this is not always true, for in some instances the umbilical area may be the only site of obvious metastatic involvement. An example of this was seen in a case reported by Witthauer.[6] Even when the diagnosis of extensive carcinomatosis is fairly definite, as in the fourth case reported here, it can be established beyond any doubt by a simple and harmless excision, under local anesthesia, of the umbilical nodule. These nodules are often quite small, averaging, in my experience, several centimeters in diameter, and must be carefully felt for. At times a distinct tumefaction may not be present; instead, there may be a poorly demarcated thickening of the subcutaneous tissue due to its infiltration by nests of tumor cells that often are surrounded by a desmoplastic connective tissue.

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2. Cullen, T. S.: The Umbilicus and Its Diseases, Philadelphia, W. B. Saunders Company, 1916.

3. Lombardi, L. E., and Parsons, L.: Carcinoma of the Umbilicus Metastatic from Carcinoma of the Stomach, Ann. Int. Med. **22**: 290 (Feb.) 1945.

4. Williams, C.: Unusual Surgical Lesions of the Umbilicus: Report of Cases of Congenital Origin, Ann. Surg. **124**: 1108 (Dec.) 1946.

5. Rochet, F., and Francillon, M.: Tumeur de l'ombilic, metastase d'un neoplasme des voies biliares, Lyon Med. **167**: 239 (March 29) 1942.

6. Witthauer, W.: Ueber einige Falle von Nabelmetastasen bei Magenkrebs (zugleich ein Beitrag zur Frage des Carcinoma bei Jugendlichen), Med. Klin. **17**: 655 (May 29) 1921.

The pathogenesis of the metastatic lesions in the umbilical region has not been clearly established. In those cases where generalized peritoneal involvement exists, it probably represents extension by contiguity. In other cases, vascular spread may be the means by which it reaches the umbilicus. It is true that carcinoma usually follows fairly definite patterns of metastatic spread, depending on the site of the primary lesion; yet, it is not too rare to find the initial locus of extension in an unpredictable and distant area. It has also been postulated that umbilical metastasis may occur through persistent paraumbilical veins. Whatever the mechanism and whatever the role of embryonic remnants, it is an established fact that the tumor cells do invade the umbilical region (fig. 2).

SUMMARY

1. Four cases of proved metastatic lesions to the umbilical region are reported.

2. The accessibility of this area to local biopsy study is stressed.

3. Careful palpation of the umbilical area for tumor nodules should be as much a part of routine physical examination as examination for an enlarged liver.

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PERFORATION OF BOWEL DURING TREATMENT OF ULCERATIVE COLITIS WITH CORTICOTROPIN

REPORT OF THREE CASES

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Corticotropin (ACTH) and, to a lesser extent, cortisone have recently been used in the treatment of nonspecific ulcerative colitis. As with other drugs used in the treatment of this disease, the results have varied widely. Pronounced improvement has been noted in some cases during corticotropin or cortisone therapy,[1] but only brief mention has been made of peritonitis and perforation during the course of therapy.[1a,d] Other reports on corticotropin or cortisone therapy have described the perforation of peptic ulcers during treatment.[2] Perforations of the small intestine have been reported in one patient with regional enteritis.[1a]

It is our purpose to report three cases of peritonitis occurring among 17 patients with ulcerative colitis treated by us with corticotropin. Thirteen patients received 25 mg. of corticotropin every six hours intramuscularly for 17 to 30 days. Four patients received 20 mg. each day by continuous infusion over an eight hour period for 2 to 14 days as described by Renold and co-workers [3] and Gordon and co-workers.[4]

REPORT OF CASES

CASE 1.—A 23-year-old unmarried actuarial student had an episode of cramps with 10 to 20 bloody bowel movements a day during an examination period in June, 1950. In February, 1951, again during a series of examinations, bloody diarrhea and cramps returned. Ten days before admission, in June, 1951, he had an explosive recurrence of low abdominal cramps and 20 to 24 bloody bowel movements a day with temperature up to 38 C (100.4 F), anorexia, and occasional vomiting; he lost 15 lb. (6.8 kg.) in weight.

On admission the temperature was 40 C (104 F) and the pulse rate 116. The patient looked lethargic and moderately ill, with dry, hot, flushed skin. General examination disclosed only mild abdominal tenderness, maximal in the left lower abdominal quadrant. There was no muscle spasm. Proctoscopic examination revealed a diffusely engorged, friable rectal mucosa, a few scattered ulcerations, opaque mucus, multiple bleeding points, and no polyps. A barium enema demonstrated destruction of mucosal pattern, irregularity of contour, and loss of haustral markings extending proximally to the hepatic flexure. Laboratory studies yielded the following findings: red blood cells, 3,900,000; hemoglobin, 11.5 gm.; white blood cells, 8,500; lymphocytes, 36%; band cells, 4%; polymorphonuclear cells, 60%; and no eosinophils. The urine was normal. The Mazzini reaction was negative. Blood urea nitrogen was 25 mg. per 100 cc. Serum albumin was 4.8 gm. and globulin 2.1 per 100 cc. Stool cultures were negative for pathogens. Blood cultures proved negative. The reaction to the skin test for lymphopathia venereum was negative.

After material for all cultures had been obtained, the patient was given chloramphenicol, 2 gm. per day, without change in signs or symptoms. Five days later, corticotropin was administered intravenously, 20 mg. in 1,000 cc. of 5% glucose during eight hours. This procedure was repeated the next day. On the third day, before corticotropin was given, the patient complained of severe pain in the left lower abdominal quadrant, which had begun suddenly about an hour before. He was cyanotic, with a pulse rate of 140 per minute. The abdomen was distended, tympanitic over the hepatic area, and markedly tender, with diffuse rebound tenderness. The white blood cell count was 4,600, with 50% polymorphonuclear cells and 40% band cells. X-ray studies demonstrated massive amounts of air under the diaphragm (fig. 1). Laparotomy allowed the egress of air under pressure, and purulent material was found in the lower part of the abdomen. This contained Escherichia coli on culture. The

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1. (*a*) Sloan, S.; Briggs, J. D., and Halsted, J. A.: ACTH Therapy for Ulcerative Colitis Complicated by Perforation of Coexisting Peptic Ulcer, Gastroenterology **18**: 438 (July) 1951. (*b*) Rossmiller, H. R.; Brown, C. H., and Ecker, J. A.: Effect of ACTH on Nonspecific Ulcerative Colitis, ibid. **17**: 25 (Jan.) 1951. (*c*) Machella, T. E., and Hollan, O. R.: Effect of Cortisone on Clinical Course of Chronic Regional Enteritis and Chronic Idiopathic Ulcerative Colitis, Am. J. M. Sc. **221**: 501 (May) 1951. (*d*) Halsted, J. A., and others: Clinical Effects of ACTH in Ulcerative Colitis, Gastroenterology **19**: 698 (Dec.) 1951. (*e*) McKell, T. E.; Tuthill, S. W., and Sullivan, A. J.: The Affective Response of a Patient with Chronic Ulcerative Colitis to Cortisone, ibid. **17**: 20 (Jan.) 1951. (*f*) Kirsner, J. B., and Palmer, W. L.: Effect of Corticotropin (ACTH) in Chronic Ulcerative Colitis: Observations in 40 Patients, J. A. M. A. **147**: 541 (Oct. 6) 1951. (*g*) Gray, S. J., and others: The Use of ACTH in the Treatment of Ulcerative Colitis and Regional Enteritis, in Second Clinical ACTH Conference, New York, The Blakiston Company, 1951, p. 473. (*h*) Elliott, J. M.; Kiefer, E. D., and Hurxthal, L. M.: ACTH in Treatment of Chronic Ulcerative Colitis, Gastroenterology **19**: 722 (Dec.) 1951.

2. Kirsner and Palmer.[1f] Beck, J. C., and others: Occurrence of Peritonitis During ACTH Administration, Canad. M. A. J. **62**: 423 (May) 1950.

3. Renold, A. E.; Forsham, P. H.; Maisterrena, J., and Thorn, G. W.: Intravenously Administered ACTH, New England J. Med. **244**: 796 (May) 1951.

4. Gordon, E. S.; Kelsey, C., and Meyer, E. S.: Adrenal Stimulation by Intravenous ACTH, in Second Clinical ACTH Conference, New York, The Blakiston Company, 1951, vol. 2, p. 30.

site of perforation was not visualized. Ileostomy was performed; after a difficult period, the patient improved.

Case 2.—A 36-year-old housewife had had recurrent bloody diarrhea during the year since the birth of her only child. She had up to 22 bowel movements per day, occasional vomiting, low grade fever, and loss of 10 lb. (4.5 kg.) in weight. This last

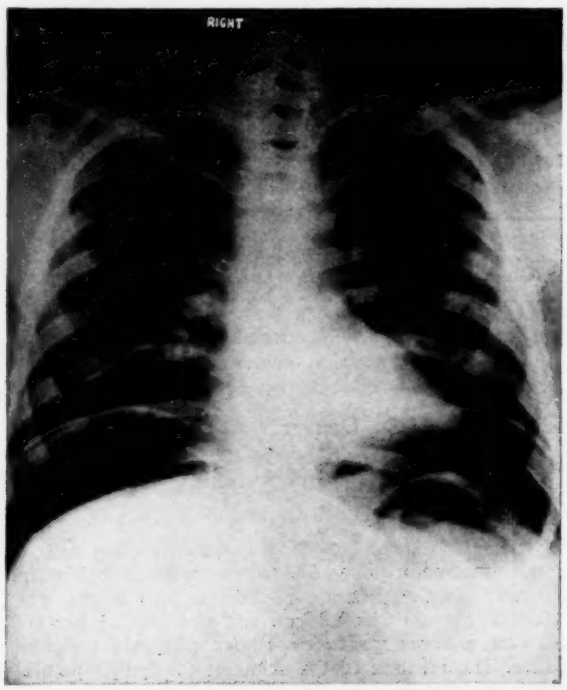

Fig. 1.—Massive accumulation of air under the diaphragm following perforation of the colon during treatment with corticotropin (case 1).

episode was of three weeks' duration, gradual in onset, and getting worse.

The patient was moderately pale and thin. The pulse rate was 110 and the temperature 38.6 C (101.4 F). Examination of the abdomen disclosed no significant abnormalities. Proctoscopic

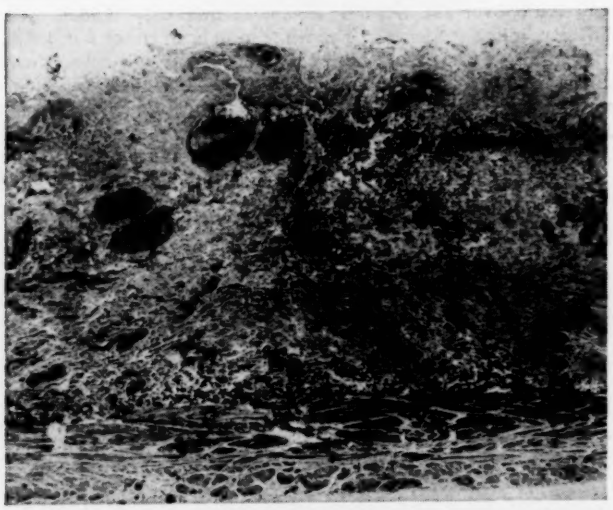

Fig. 2.—Edema and great vascularity of the mucosa and submucosa in a postmortem section of the colon (case 3).

study revealed a friable, freely bleeding mucosa, with overlying mucopurulent material. A barium enema demonstrated deeply ragged edges and absence of normal mucosal markings in the entire colon. Laboratory studies disclosed the following findings: red blood cells, 3,800,000; hemoglobin, 11 gm. per 100 cc.; white blood cells, 13,000; polymorphonuclear cells, 45%; and band cells, 33%. The urine was normal. Stool examinations were negative for pathogens.

Terramycin and methantheline bromide (banthine,® beta-diethylaminoethyl xanthene-9-carboxylate) were given. The number of daily bowel movements decreased to 8 for a few days but then mounted to 20, while the temperature rose to 39 C (102.2 F) daily. After five days of placebo (isotonic sodium chloride solution) injections, 25 mg. of corticotropin was given intramuscularly every six hours. Within 24 hours, the number of bowel movements diminished to a daily average of nine and the temperature fell to normal. Evidence of physiological activity of corticotropin included rounding of the face, elevation of the diastolic pressure, and decrease of eosinophil count to zero. Nevertheless, tachycardia, bloody diarrhea, and abdominal cramps continued. After two and a half weeks of intramuscular administration of corticotropin, the temperature rose daily to

Fig. 3.—Postmortem section showing acute inflammation penetrating all layers of the bowel wall (case 3).

38.5 C (101.3 F), with persistent tachycardia and greater shift to the left in the differential count, although the total white blood cell count reached only 9,400. Severe pain required the use of morphine, and vomiting became more frequent. The abdomen was tense and distended and slightly tender in the left lower quadrant. Ileostomy was decided on because of the worsening of the patient's condition despite intensive medical therapy. Operation was performed four days after cessation of corticotropin therapy. Several loops of jejunum were seen to be bound to each other and to the transverse colon by thick fibrinous adhesions. Two separate ½ in. (1.3 cm.) perforations were seen in the transverse colon, and these were plicated. Ileostomy was performed. The postoperative period was difficult and complicated by thrombophlebitis, ileocutaneous fistula, abdominal wall abscess, and partial small bowel obstruction. The patient was subsequently readmitted for total colectomy.

CASE 3.—A 20-year-old girl gave a history of three weeks of bloody diarrhea with fever, anorexia, 20 lb. (9.1 kg.) weight loss, and tenesmus, all of which began suddenly on the termination of her engagement to be married. On admission, the girl was depressed, querulous, thin, and acutely ill, with a temperature of 38.7 C (101.7 F) and a pulse rate of 120. Results of general examination, including that of the abdomen, were otherwise negative. Proctoscopic study revealed a friable, bleeding mucosa typical of ulcerative colitis. A barium enema showed a contracted colon, polypoid changes, and roughened borders of mucosa, everywhere except in the ascending colon. Laboratory studies disclosed the following findings: red blood cells, 4,100,000; hemoglobin, 14 gm. per 100 cc.; and white blood cells, 11,100, including 46% band forms, 9% metamyelocytes, 4% myelocytes, and 2% eosinophils.

The course during the next 15 days was steadily downhill despite the use of several antibiotics, 2,000 cc. of whole blood, methantheline and meperidine (demerol®) hydrochloride, for abdominal pain. The temperature ranged from 38.5 C to 40 C (101.3 to 104 F) and the number of bowel movements from 15 to 25 each day. The abdomen, however, remained soft and flat. On the 16th day the rectal bleeding was profuse, the abdomen painful, tender, and distended, the blood pressure 100/50, and the pulse rate 120. Twenty milligrams of corticotropin was given in eight hours in an intravenous infusion of 5% glucose. Within the next 12 hours frank congestive heart failure with pulmonary edema developed, as well as paralytic ileus. Digitalization helped the former, and cessation of treatment with meperidine and banthine® was associated with the return of bowel sounds and bloody diarrhea and the disappearance of abdominal distention. The hypochloremia and hypokalemic alkalosis responded to electrolyte adjustment in the next five days. On the 21st day the use of corticotropin was resumed, 25 mg. intravenously each day for four days, then 40 mg. the next two days. The next night the abdomen was distended, rigid, and silent, the blood pressure unobtainable, and the facies cyanotic. The rectal discharges were grossly bloody. Six hundred cubic centimeters of plasma and 1,500 cc. of whole blood were given. The patient died on the 30th hospital day. It is to be noted that the corticotropin had no effect on the temperature, appetite, or abdominal distention and rigidity.

At postmortem examination the abdomen was greatly distended and tense, and on incision of the peritoneum no gas escaped. The cavity contained about 400 cc. of turbid straw-colored fluid, from which Streptococcus hemolyticus, Aerobacter aerogenes, and Monilia albicans were grown. There was marked distention of the small and large intestines, and acute fibrinous peritonitis was present, most severely in the left paracolic region. A small perforation, found in the pelvic colon, was considered to be of postmortem occurrence.

Microscopically the mucosa was largely replaced by vascular granulation tissue (fig. 2); there were scattered islands of surviving epithelium, frequently related to lymphoid follicles. There were numerous foci of hemorrhage, and several subserosal vessels showed necrotizing vasculitis and organizing thrombi. In some areas (fig. 3) inflammatory cells penetrated to the serosa, where there were a few strands of fibrin. The paucity of fibrosis in the intestinal wall led to the final diagnosis of acute ulcerative colitis.

COMMENT

The use of corticotropin in cases of ulcerative colitis has been prompted by the widely recognized concurrence of this disease with rheumatoid arthritis and erythema nodosum, both of which have responded to treatment with the hormone. Its use is supported by observations that, in patients severely ill with ulcerative colitis, adrenal cortical functions are defective.[5] There is also widespread acceptance of the usefulness of corticotropin in many diseases of unknown causation, including those of the collagen system. Levine and co-workers [6] have indicated that ulcerative colitis may belong in that category.

It is now well established that corticotropin therapy suppresses inflammatory reaction.[7] It inhibits proliferation of fibroblasts and retards the healing process in man as well as in the experimental animal.[8] Indeed, it has been noted that, in at least two groups of diseases in which the cellular response is important in healing, the disease process is progressive during corticotropin or cortisone therapy: (*a*) previously inactive foci of tuberculosis have become activated [9] and (*b*) bacterial and primary atypical pneumonia have become worse.[10]

With respect to our three cases of ulcerative colitis, it is impossible to state exactly how the corticotropin therapy affected the outcome. In case 2, in which corticotropin was given for 20 days, the abscess formation proceeded in the absence of the usual signs and symptoms of localized peritonitis. Generalized peritonitis has also occurred without clinical manifestations during corticotropin therapy.[3]

The condition in cases 1 and 3 was typical of fulminating ulcerative colitis. In case 1, however, the patient was only moderately ill. His clinical appearance and proctoscopic findings were such that one would not have anticipated perforation. Nevertheless, after two days of intravenous corticotropin therapy, the patient's colon suddenly became perforated. It may be argued that this event was unrelated to the brief period of corticotropin therapy, but Renold and co-workers [3] and Gordon and co-workers [4] have demonstrated profound physiological effects from as little as a single intravenous infusion containing 20 to 25 mg. of corticotropin.

The patient in case 3 was critically ill throughout her hospital course and died of peritonitis after seven days of intravenous corticotropin therapy. It has been the general experience that a patient with this type of condition often dies, usually of peritonitis, despite various forms of therapy. Some authors, however, have described marked improvement with corticotropin or cortisone therapy in patients severely ill with ulcerative colitis. Machella and Hollan [1c] reported that two critically ill patients responded well. Halsted and co-workers [1d] stated that one patient with fulminating ulcerative colitis became "spectacularly better within 18 hours after ACTH." McKell and associates [1e] noted dramatic improvement in a patient with ulcerative colitis within 48 hours after cortisone therapy. Rehfuss [11] stated that corticotropin therapy is "most effective in acute fulminating cases" of ulcerative colitis.

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11. Rehfuss, M., in discussion of the paper by Elliott, Kiefer, and Hurxthal.[1b]

The colon in patients with fulminating ulcerative colitis has been vividly described by Crile and Thomas [12] as being identical with a "third degree burn covered by a fecal poultice," the bowel mucosa destroyed, the muscular coats necrotic, and the vessels thrombosed, the colon being in effect a serosal sac. Peritonitis with or without frank perforation has been the commonest cause of death in these patients. The over-all incidence of this complication in Bargen's [13] series of 1,500 cases of ulcerative colitis was only 2%. The incidence of death from peritonitis in Crile's series of 31 cases of acute fulminating ulcerative colitis was 33%.[12] On the other hand, Lahey [14] stated merely that "perforation is not a common complication" of ulcerative colitis. Partly for this reason and partly because of the small size of our series (17 cases) the statistical significance of three instances of peritonitis cannot be established.

Because of the pathologicoanatomic changes in the colon in cases of ulcerative colitis and because of the known retardation of the healing processes by corticotropin therapy, it is reasonable to assume that the use of this hormone contributed to perforation and peritonitis. The extremely thin, friable bowel wall makes this very likely in cases 1 and 3 and similar cases.

The occurrence of peritonitis in 3 patients among a series of 17 with ulcerative colitis treated with corticotropin raised a doubt as to the advisability of indiscriminately using this hormone in all cases of ulcerative colitis. The good results reported by others must be considered. The hazard of corticotropin therapy in the chronically ill patient with marked increase in organized inflammatory cellular change in the colon is probably very different from that in the acutely ill patient with fulminating colitis with sudden onset of fever, marked prostration, shift to the left in the differential white cell count, and poorly organized exudative inflammatory reaction in the colon. In the latter group, the potential risks of corticotropin therapy are grave enough to contraindicate its use.

SUMMARY

Among 17 patients with ulcerative colitis treated with corticotropin (ACTH), a localized perforation of the colon developed in 1 and acute perforation with generalized peritonitis developed in 2. The clinical signs of acute perforation were not suppressed. In cases of acute fulminating ulcerative colitis, in which necrosis and poorly organized exudate are present in the bowel wall, the rationale for the use of corticotropin is questionable and the risk of such complications as peritonitis and perforation is grave.

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TREATMENT OF BRONCHIAL ASTHMA

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Although the word asthma is popularly associated with wheezing in general, bronchial asthma, in our opinion, is an allergic disease, with generalized wheezing, dyspnea, orthopnea, and cough, usually associated with seasonal or perennial rhinitis. The wheezing is due to partial obstruction caused chiefly by edema and mucus. The watery material tends to be expelled during expiration; thick tenacious sputum and mucous plugs may remain. Space will not permit discussion regarding etiology, diagnosis, and differential diagnosis.[1]

PREVENTIVE TREATMENT OF BRONCHIAL ASTHMA

Children of allergic parents are likely to have allergic diseases. They need shielding from potent allergens, and allergic parents should observe the following precautions:

1. Dogs and cats should be removed from the home. Even if results of tests are negative, the dander is likely to aggravate symptoms, and rhinitis or asthma may follow.

2. House dust should be kept at a minimum. The mattress and pillows should be rubber or encased in dustproof, zippered material. Plastic covers over stuffed furniture are valuable. To prevent dust from falling to the floor, the bottoms should be boarded up by pieces of thin linoleum. Rubber-filled furniture and rubber rug pads are recommended. Linoleum is excellent. These homes should be as clean as hospital rooms (witness the rapid recovery that usually occurs when an asthmatic patient enters a hospital and the relapse in some patients when they return to their "dusty" homes).

A vacuum cleaner with attachments can suck dust from under sofa cushions and from drapes and rugs. Whisk brooms merely move dust from one place to another. Kapok, a pernicious allergen, should be avoided throughout the house; it is found in many show pillows and in furniture and mattresses.

Stuffed quilts, stuffed toy animals, heavy drapes, and bedroom carpeting should also be avoided. House dust not only is an allergen but can also be a cause and carrier of disease.[2]

3. The house, especially the basement, should be kept dry, as dampness tends to increase the number of molds.

4. The mother should use orris-free cosmetics.

5. Foods may be important, and one new food (not a mixture) should be added at least three to four days

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1. Unger, L.: Bronchial Asthma, Springfield, Ill., Charles C Thomas, Publisher, 1945.

apart. If allergic symptoms occur, e. g., wheezing, cough, rhinorrhea, or abdominal pains, this new food should be avoided for a week or two and then tried again. Egg is a frequent cause of asthma and angioneurotic edema. It should be introduced into the diet cautiously after the infant is a year old, but never in the raw form, as severe shock can occur. Milk rarely causes asthma.

6. Pollen causes hay fever, and asthma may follow. Since the pollen count is usually greater in rural districts, those who live in cities usually have less symptoms. Before potentially allergic children go to summer camps, tests for pollens should be carried out. The scratch method takes a few minutes and is safe. If the child gives positive reactions to ragweed pollen extract, he should be kept away from ragweed-infested areas. If the reaction to grass pollen is positive, the child should avoid camps during the grass season. Camp sites are often full of weeds, which may grow through holes in the floor of the dwellings so that the child is exposed to pollen 24 hours a day. Coke [3] of England said, "Little children should not be encouraged to run about among high grass when it is pollenating. Their noses are at about the same level as the tall timothy grass and the meadow foxtail." Ragweed-positive children may go to camp during the grass season and vice versa.

7. These youngsters should avoid dusty work, such as is done by farmers, bakers, furriers, upholsters, grain mill workers, or florists, and should not work around animals. It is easy to avoid these occupations; it is difficult to change when one is an adult.

8. If a child (or adult) has a "cold" and usually has asthma after such a cold, an immediate intramuscular injection of 0.50 to 1.0 cc. of epinephrine in oil will usually prevent the asthma, though the cold itself is not affected.

9. Children who have shown allergic symptoms, e. g., rhinitis, hay fever, or "eczema," should be promptly and thoroughly skin-tested. Bronchial asthma is not a mild condition and can lead to chronic invalidism, with emphysema and chest deformities. Scratch tests should be done first; if sufficient information is not obtained, tests by the intradermal method should follow. Children (and adults) with hay fever should receive injections of the appropriate pollen extracts. Such hyposensitization will almost always prevent the onset of asthma.

10. Last, but not least, these children need good hygienic care, including nutritious food and sunshine. They should also receive the usual immunizations, especially for tetanus, diphtheria, and whooping cough. Diseased tonsils and adenoids should be removed, but such removal rarely prevents or lessens allergic symptoms. If allergic parents carry out the above suggestions, either asthma will not occur, or, if it does, attacks will be mild and easily controlled.

SPECIFIC TREATMENT OF BRONCHIAL ASTHMA

The specific treatment consists of (*a*) elimination and (*b*) hyposensitization and is usually successful in eliminating or, at least, lessening symptoms.

Elimination.—Removal of the cause, if complete, almost always induces prompt relief from symptoms. This procedure constitutes a clinical "cure," but, immunologically, there is no real cure because symptoms will usually recur on reexposure. Since the cooperation of the patient is essential, the physician should furnish a report of his findings to the referring doctor and the patient and should tell the patient, in writing, how to avoid the offending allergens.

Pollen from trees, grasses, and weeds is the cause of seasonal hay fever, with or without asthma. The distribution and seasons vary in different sections, and the physician must learn the local botany. Exposure can be lessened by (*a*) weed destruction (the ideal), (*b*) vacation from infested regions during pollenation, (*c*) closing windows and doors or wearing masks, and (*d*) filters in the bedroom window.

The outdoor seasons of molds and smuts are not as clear-cut, and certain parts of the country are dry and have fewer fungi. Indoor molds may be abundant in bedding, rotting shoes and clothing, behind pictures, and especially in damp basements; the dampness can be relieved by the use of sacks of calcium chloride or a dehumidifier. Smuts are common in or near farms, grain mills, and similar industries.

House dust and feathers have already been mentioned, and we have emphasized the use of rubber in bedding, furniture, and under rugs. Kapok is a potent allergen and should be barred from the home. Household pets should not be permitted in the home. Among other inhalant allergens that may require avoidance are cottonseed, orris root, karaya gum, gum acacia, castor bean, pyrethrum, and certain powdered drugs.

Foods can also cause asthma. Eggs or milk may be the allergens, and patients must be given diets that list foods they may eat and foods they may not. Heating decreases allergenicity, and less sensitive persons can sometimes eat small amounts if the food is well cooked.

Avoidance is sufficient for drug allergy. Acetylsalicylic acid may cause severe asthma, and the patient must avoid it and all mixtures that contain this drug; the patient must also keep asking whether it is part of any medicine prescribed for him.

Hyposensitization (*Desensitization*). — Indication: Hyposensitization is advised for important inhalant allergens that cannot be sufficiently avoided, e. g., pollens, fungi, house dust, feathers, animal danders, cottonseed, and orris root. We also administer injections for allergy to egg and wheat. (Many allergists believe it is not necessary to give injections for these two foods, and others try the oral method, which gives only mediocre results.) Hyposensitization usually increases the patient's resistance so that he can withstand ordinary amounts of his offending allergen or allergens. It is rarely possible, however, to immunize to such an extent that a child who is sensitive to egg can eat a raw egg or a man who is sensitive to horses can curry a horse.

Technique: The initial dosage is usually based on the size of the reaction to the skin test. If the erythema result-

2. Unger, A. H.: House Dust as a Cause and Carrier of Disease, Mississippi Valley M. J. 73: 14, 1951.

3. Coke, F.: Asthma, ed. 2, Bristol, England, John Wright & Sons, Ltd., 1939, p. 95.

ing from a scratch skin test is as large as a nickel, a weak dilution is best, e. g., 1:100,000 or 1:1,000,000. If the reaction to the scratch test is negative but the reaction to the intradermal test (usually 1:1,000) is positive, a 1:10,000 dilution is usually safe. With certain potent allergens, e. g., horse dander, egg, cottonseed, and the brand of house dust extract made by Endo Products, weaker dilutions, e. g., 1: 1 billion should be used at the start.

The important principles are as follows: 1. Proper extracts should be used. (The solutions must be specific, e. g., ragweed for ragweed cases.) 2. In pollen-sensitive patients the doses should be increased on a time schedule so that the top amount is reached just before the pollen season begins. 3. Subcutaneous injections should be given with tuberculin syringes and ½ in. (1.27 cm.), 27-gage needles, with a 5% dextrose-phenol extracting fluid. This solution is as stable as those made with glycerine and is preferred because it is not irritating. 4. The extracts should be made up so that doses can be increased or decreased to meet the patient's sensitivity. We usually begin with 0.10 cc., followed by 0.15, 0.22, 0.30, 0.45, 0.65, and 0.85 cc. If no reactions occur, we increase from 0.85 cc. of this dilution to 0.10 cc. of the next stronger dilution, then 0.15 cc., and so on. The next solutions follow in succession, e. g., 1:1,000, then 1:100, and then 3%. With the latter two dilutions, increases should be 0.02 cc. each time.

With pollens the injections are best started before the hay fever season, then continued with doses reduced approximately 25% during the pollen season, then carried on all year round (perennial treatment) with increases of 0.02 to 0.05 cc. each time. Injections are usually given twice a week at first, later once a week, then every two weeks, and finally every three weeks.[4] The perennial method is preferred because higher doses can be reached and results have been much better than with the preseasonal injections. If the patient has hay fever only, treatment with the injections can often be stopped after two to four years; however, when pollen asthma is also present, treatment should be continued year after year. The results are usually excellent, but asthma usually returns when treatment with the injections is stopped.

Hyposensitization with allergens other than pollen is given in much the same way, but, since there is little need for a time schedule, the intervals between injections can usually be arranged to suit the patient—usually once or twice a week to begin with.

The top dosages vary, but those who can take large amounts almost always obtain the best results. Some allergists give only minute doses of house dust or pollen extracts, and we have obtained good results in a few patients whose doses could not be increased.

When there is an allergy to egg or wheat, we instruct the patient to avoid these foods until the 1:1,000 dilution has been reached. The patient then tries small and increasing amounts of food that contain egg or wheat, beginning with a small piece of cake.

4. Unger, A. H., and Unger, L.: Treatment of Bronchial Asthma, Gen. Practitioner 4: 79, 1951. Unger.[5]

5. Goodall, R. J., and Unger, L.: Continuous Intravenous Aminophyllin Therapy in Status Asthmaticus, Ann. Allergy 5: 196, 1947.

With care, the results from hyposensitization are usually good. To prevent reactions, we advise the precautions outlined on pages 400 to 403 in "Bronchial Asthma." [1]

SYMPTOMATIC TREATMENT

Nonspecific treatment does not offer the same hope for complete relief from symptoms as do the specific measures just discussed, but symptoms must be relieved as they occur. Only worth-while measures will be mentioned.

Treatment of the Asthmatic Attack.—Treatment varies with the severity of the attack and with the age and other factors. The edema and thick mucus are lessened by the use of epinephrine and ephedrine, along with iodides, syrup of ipecac, and bronchoscopic aspirations. Various combinations of aminophylline, ephedrine, and mild sedatives are also useful. Antihistaminic drugs are of limited value.

Hospitalization is strongly advised if attacks have lasted for three or more days. Medication is carried out more successfully in the hospital, and complications, e. g., infectious or cardiac, are easily detected and treated. In addition, hospitalization may remove the patient from his allergens and from emotional stresses in the home.

Every hospital should have at least two or three rooms designed for asthmatic patients. Wesley Memorial Hospital (Chicago) has 12 such beds, including six single rooms and three with 2 beds each. The bedding in these rooms is rubber, and the floors are covered with inlaid linoleum. The chairs are plastic covered, and thin curtains are changed every two weeks. Each room has an air filter, which removes 95% to 99% of atmospheric pollens and fungi. The filter is placed just above the radiator, and on cold days warm air is drawn in and given out. Smoking, dry dusting, and flowers are not permitted in these rooms.

These "asthma" rooms have been occupied by over a thousand asthmatic patients during the past 10 years. In most cases symptoms disappear within a few days; however, if the asthma persists for a week or more after admission, inhalant allergens cannot be the entire cause —some other factor must be present. This may be infectious, psychosomatic, food allergy, or some nonallergic disease.

Reassurance is most important. The patient must be told, calmly and with conviction, that he should soon be able to lie down without dyspnea. In some cases the patient will not relax until the family has been sent home.

Medication.—Aminophylline: Aminophylline is, in our opinion, the best drug for hospital use, especially for those who have had too much epinephrine. In severe attacks, one should slowly inject (about four to five minutes) 10 cc. of aminophylline (0.24 gm., or 3¾ grain) intravenously, then every day give intravenously 0.48 gm. (7½ grain) in a liter of 5% glucose in distilled water at 60 drops per minute. If asthma persists after three to four days, the continuous method is advised (0.50 to 1.0 gm. of aminophylline in each liter of 5% glucose at 28 to 30 drops per minute) for as long as necessary, even up to a week or longer. As improvement

occurs, the amount of aminophylline is reduced. Few patients fail to be helped by this technique.[5] Aminophylline is a safe drug to be used in cases of bronchial asthma, provided it is injected slowly and in doses known to be safe; it is rare cause of death per se.

Aminophylline is also valuable administered per rectum. In adults, one may instill 10 grains (0.60 gm.) dissolved in 20 cc. of tap water. For children, 5 grains (0.30 gm.) is sufficient. Rectal suppositories of 7½ and 3¾ grains (0.50 and 0.24 gm.) act more slowly. Aminophylline is much less effective when given orally, and intramuscular use is too painful.

Epinephrine: Epinephrine (1:1,000) is also excellent for use in adults and is preferred in children. The usual dose is 0.40 to 0.50 cc. for adults and 0.15 to 0.30 cc. for children. Larger amounts increase tachycardia and tension. We suggest smaller doses, repeated as necessary, especially in patients who also have hypertension. Many patients have already had too much epinephrine and are "epinephrine-fast." In such cases use of the drug usually becomes effective again if withheld for a few days. Epinephrine is usually injected subcutaneously, but in severe conditions, even with "epinephrine-fastness," one can often obtain relief by adding 1.0 cc of the 1:1,000 dilution to the slowly dripping liter of 5% glucose, with or without added aminophylline.

Epinephrine in oil (1:500) may be injected into the upper outer quadrants of the buttocks twice daily in doses of 1.0 cc. for adults and 0.50 cc. for children. This gives prolonged action and is therefore contraindicated if hypertension is present. A new remedy, "sus-phrine," (1: 200 suspension of epinephrine in a glycerin base), is also useful.[6] It is given subcutaneously in doses up to 0.40 cc., and its action continues for about as long as does that of epinephrine in oil. We prefer this combination in children.

Epinephrine (1:100) by inhalation (which has almost entirely replaced the old stramonium vapors) has little place in hospital therapy but is recommended for mild asthma. Many patients carry the nebulizer wherever they go and reach out at night for a few inhalations. We prefer the 1:100 solution (never stronger) and a good nebulizer. The patient must be taught to use it only when necessary. We do not agree with the warning by Benson and Perlman, who suggested that this spray contributed to the death of 48 of 648 asthmatic patients.

Sedation: Morphine and meperidine hydrochloride should not be used during an attack of asthma, and we seldom prescribe any sedative stronger than 50 to 100 mg. of an antihistaminic drug, e. g., diphenhydramine (benadryl®) hydrochloride or up to ½ grain of phenobarbital. The patient must be encouraged to cough up the heavy sticky mucus that interferes with his breathing. Morphine slows respiration and lessens the cough reflex and therefore increases anoxia. Death has frequently occurred in asthmatic patients to whom morphine was given. Most allergists no longer use morphine because they know that, no matter how severe the attack, the patient will almost always recover if that drug is not used. This statement does not mean that death will always follow the use of the drug; in fact, older physicians still contend that the use of morphine has stopped attacks when other measures failed. However, all too often administration of the drug quiets the patient permanently. Vaughan [7] correctly said: "With regard to asthma, the statement is sometimes made that morphine should not be used except as a last resort. The writer feels that this is precisely the time when morphine should not be used. . . . He [the patient] is already fighting for his breath with every ounce of energy that he has and the slowing of the respiration from morphine may be just enough to determine death from asphyxia."

The other strong sedatives are not as harmful but should also be avoided, because it is better to have a noisy patient than one who is quiet and unable to expectorate. Alcohol is an excellent and a safe sedative. It can be given at night, e. g., 1 to 2 oz. (30 to 60 cc.) of whiskey, plus 10 grains (60 gm.) of acetylsalicylic acid (unless sensitivity to the latter exists). Alcohol often works well when a liter of 5% alcohol in glucose is injected intravenously, 120 to 130 drops per minute. When the patient shows signs of inebriation, the rate is slowed to 80.[8]

Ether: Ether per rectum is being used less frequently (2 oz. with 4 oz. [120 cc.] of liquid petrolatum). Full ether anesthesia (30 to 40 minutes) may end a prolonged attack of asthma. Some indicated surgical procedure, e. g., cholecystectomy, can often be combined with the anesthesia.

Antibiotics: Antibiotic therapy is necessary for any coexisting infection; the attack will usually continue until the infection has been overcome. Infection is indicated by fever, leukocytosis, increased sedimentation rate, localized rales, or x-ray findings. Penicillin is most widely used, but sensitivity tests may suggest streptomycin, aureomycin, chloramphenicol, terramycin, or sulfonamides. Many hospitalized patients whose condition does not clear up in a week have an infectious complication.

Sodium and Potassium Iodide: These agents help because they loosen the sputum. Sodium iodide given intravenously (1 to 2 gm.) is also useful. For many years we have had excellent results, especially in the more chronic cases, by adding apomorphine hydrochloride, a good expectorant, as follows:

Apomorphine hydrochloride	2 grains (0.13 gm.)
Potassium iodide	5 drams (8.86 gm.)

Syrup cherry in sufficient quantity to make 4 oz. (120 cc.)

One teaspoonful three to four times daily (the amorphine should first be dissolved in 2.0 cc., of distilled water, then added).

Ipecac Syrup: Ipecac syrup, one teaspoonful every hour until emesis, is excellent for use in the acute asthma of children. Thick sputum is often excreted with the vomitus.

Glucose: Glucose is a valuable food, especially because it replaces glycogen driven from the liver by epinephrine. It can be given intravenously, by the addition of 5 oz. (150 cc.) of glucose to a quart of fruit juice given daily.

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6. Unger, A. H., and Unger, L.: Prolonged Epinephrine Action: Report on Use of Epinephrine Suspension, Ann. Allergy **10**: 128, 1952.
7. Vaughan, W. T.: Practice of Allergy, St. Louis, The C. V. Mosby Company, 1939, p. 920.
8. Brown, E. A.: Use of Intravenous Ethyl Alcohol in Treatment of Status Asthmaticus, Ann. Allergy **5**: 193, 1947.

Oxygen: Oxygen (with or without helium) is rarely helpful in uncomplicated bronchial asthma, even if severe, but its use is essential in cyanosis. When pulmotor squads are called, they probably harm asthmatic patients because the excitement usually increases the patient's terror and his asthma.

Ephedrine: Ephedrine given in doses of ¼ to ½ grain (0.16 to 0.32 gm.) helps mild and moderate asthma but is of little aid in severe attacks. Its continued use can slow the urinary stream in older men. Because it causes nervousness and insomnia, it is often combined with a sedative, with or without the addition of aminophylline and/or an antihistaminic drug. Methoxyphenamine ("orthoxine") hydrochloride is one of several synthetic compounds that act like ephedrine yet do not increase blood pressure.

Isopropylarterenol Hydrochloride: This drug has been widely used by inhalation in a 1:200 dilution or under the tongue in doses of 10 to 15 mg. It has an epinephrine-like structure but does not raise blood pressure; it dilates the bronchi but does not contract blood vessels and lessen edema as epinephrine does. Therefore, its action seems better in some patients; in others the use of epinephrine is more successful. Despite claims to the contrary, use of the drug does increase nervousness in many patients.

Antihistamines: Antihistaminic drugs seem of little value in patients with severe asthma except that the antihistamines that have a sedative action, e. g., diphenhydramine hydrochloride, work well at night. The combination of an antihistaminic drug with aminophylline is useful in milder attacks, especially in patients with pollen asthma.

Ammonium Chloride: Ammonium chloride is a good expectorant given in doses of 0.3 to 1.0 gm. Potassium iodide is preferred.

Arsenic: Potassium arsenite (Fowler's) solution has been used on and off for many years. Its mode of action in asthma, if any, is unknown. Some patients have derived distinct, though temporary, benefit from a mixture containing this drug, potassium iodide, and other ingredients. Arsenic is a drug to be watched as attested by the occurrence of arsenical dermatitis in two patients who received this "Gay" mixture for asthma.[9]

Bronchoscopic Aspiration: Bronchoscopic aspirations can sometimes save a life, especially when the patient is too feeble to expel sticky secretions. The removal of 20 cc. of thick sputum from the bronchi of an elderly moribund patient enabled her to walk out of the hospital about a week later. The use of morphine must be avoided with this procedure, and sedation should be minimal.

Digitalis: The use of digitalis is of no value in asthma unless there is decompensation or auricular fibrillation.

Corticotropin and Cortisone: We have delayed discussion on the use of corticotropin (ACTH) and cortisone in patients with asthma because we believe these hormones should be tried only if the standard measures, e. g., administration of aminophylline and epinephrine, have failed. They should not be used routinely nor should their use supplant careful allergy surveys and therapy.

In the hospital we usually begin with 20 mg. of corticotropin added to each liter of aminophylline in 5% glucose, which is given by slow continuous intravenous drip. The patient usually receives about 2 to 3 liters per 24 hours (40 to 60 mg. of corticotropin). This is less expensive than giving the usual 25 mg. doses every six hours. Results have been brilliant in many patients with severe status asthmaticus. The asthma usually lessens promptly, and the patient feels better, eats better, and gains weight. If the patient continues to improve, the dose of corticotropin is gradually reduced, or one can substitute cortisone, given by mouth, usually beginning with at least 25 mg. every six hours. This therapy must be continued over a long time, because the asthma usually returns if the treatment is suddenly stopped. In some patients the therapy has been continued for a year or more. The usual precautions, e. g., low sodium intake, are necessary.

These hormones, then, provide an extra weapon, a powerful one that may promptly ease the suffering of an asthmatic. Before starting this method, the physician should weigh the advantages (more or less prompt relief in many cases) against the disadvantages (prolonged expensive therapy, difficulty in stopping, possible reactions, and rarely any permanent relief from symptoms). When the physician considers the matter thoughtfully, he will usually give corticotropin and/or cortisone when he is forced to do so by fear of imminent death or because of the presence of status asthmaticus that has resisted usual therapy. However, he will not start treatment with these hormones, nor will he use them to replace agents the use of which is based on the allergy survey.

House Calls.—One who undertakes the care of an asthmatic patient should, if possible, be responsible for house calls. On the physician's arrival, the patient is usually sitting up and gasping for breath. We, therefore, bring the following equipment: eccentric all-glass 10 cc. syringes, with 25 gage, 1 in. (2.5 cm.) stainless steel needles (for aminophylline); 2 cc. syringes with 1½ in. (3.8 cm.), 21 gage needles (for epinephrine in oil); and 1 cc. tuberculin syringes with 27 gage, ½ in. (1.3 cm.) needles (for 1:1,000 epinephrine or "sus-phrine"). These syringes and their needles are wrapped separately in paper and are autoclaved at the office. Metal containers can also be used. The eccentric tip on 10 cc. syringes is useful for entering the vein; metal-tipped syringes may obstruct the view.

In adults, we usually begin with the administration of 10 cc. of aminophylline intravenously (slowly), then follow with 1.0 cc. of epinephrine in oil (buttock) or with 0.30 to 0.40 cc. of "sus-phrine" (subcutaneously). We usually give children 0.20 cc. to 0.35 cc. of 1:1,000 epinephrine, subcutaneously, and either 0.5 cc. of epinephrine in oil or about 0.20 cc. of "sus-phrine." When the physician is prepared for these emergencies, the patient is more quickly relieved.

After the injections are given, we inspect the patient's home for the presence of dogs or cats and such items as feathers, kapok, molds, and house dust, as well as for psychological factors, e. g., excessive sympathy on the part of the family or undue fear by the patient. The attack is usually overcome by administration of the above injec-

9. Pascher, F., and Wolf, J.: Cutaneous Sequelae Following Treatment of Bronchial Asthma with Inorganic Arsenic: Report of 2 Cases, J. A. M. A. **148**: 734 (March 1) 1952.

tions plus the calmness and confidence of the physician; if severe asthma continues, the patient should be sent to the hospital.

Treatment of Asthma Between Attacks (Office Procedures).—When the paroxysm has completely or partially subsided, efforts should be made to prevent or at least lessen future attacks. Indifference or a "wait and see" attitude invites emphysema and chronic asthma. The complete allergy survey should be carried out at this point (history, examination, skin tests, and clinical trials). If this has already been done, the survey should be studied again with additional tests, if necessary, to see why the recent attack occurred. Hyposensitization should be started, if indicated, and the offending allergens removed as completely as possible.

In addition, the patient's symptoms, if any, require the measures already mentioned, especially treatment with the iodides, apomorphine hydrochloride, and the various ephedrine compounds. The patient may be taught to inhale with 1:100 epinephrine or 1:200 isopropylarterenol hydrochloride, to use aminophylline rectally, or to take enteric-coated ephedrine compounds at bedtime to carry him through the night.

The use of vaccines may or may not help but should be tried. Most other interval measures have been disappointing. These include the use of autohemotherapy, histamine, histaminase, endocrine products (except where specifically indicated), calcium, tuberculin, peptone, and parasitic extracts and venoms. Temporary improvement has occurred after the use of hyperpyrexia and x-ray exposures to the chest or spleen.

Removal of foci of infection is indicated per se, but the asthma is rarely benefited. The wholesale removal of teeth, tonsils, gallbladders, and appendixes is to be deplored. Neurological surgical procedures are dangerous and usually of little avail.

The emaciated patient should be encouraged to eat heartily and to avoid only those foods that he knows after several trials lead to asthma. (He must not be deprived of foods merely because of positive reactions to skin tests.) Multiple vitamins are usually added. While asthmatic patients must avoid exertion during periods of dyspnea, they should be encouraged to live as normally as possible. They should walk, perhaps play golf on flat courses, and work to the limit of their respiratory capacities. Morale must be maintained. Change of climate should be advised only after a careful allergy survey. In suggesting removal, one must weigh the advantages, e. g., lessening of exposure to certain pollens and fungi, against the possible disadvantages, e. g., loss of income, separation from the family, and possible failure to improve after the change has been made. Warmer climates may help those with cardiac and infectious complications. Ragweed sufferers obtain excellent relief when they move from the ragweed belt to such places as west of the Rocky Mountains or southern Florida. Unfortunately, many patients move here or there, with little reason, and many of these obtain little or no relief. Those who benefit from change of climate are usually those with milder asthma, many of whom could have been helped by adequate treatment in their own vicinity.

Patent medicines are mentioned but only to be condemned. They tend to self-medication and to habit formation; they are often more expensive; some contain hidden drugs that may cause or increase asthma, e. g., acetylsalicylic acid in alka-seltzer®; and their use delays those specific measures, already discussed, that alone can more or less permanently relieve symptoms.

TREATMENT OF CONTRIBUTORY FACTORS

While attacks of bronchial asthma are usually brought on by such specific allergens as pollen, secondary factors aggravate the symptoms; these are psychological, endocrine, infectious, and mechanical.

Psychological Factors.—Psychological factors are important. There is a pronounced nervous tension in many asthmatic patients, probably due to fear, overmedication, and to the dyspnea and wheezing. Oversympathy on the part of the family often increases symptoms. A reassuring physician can do much to lessen the nervous tension. It may be necessary to remove the patient from the family or the family from the patient. The literature is full of references to the psychosomatic aspects of asthma, among them an excellent book on that subject.[10] Mitchell, Curran, and Myers allow their patients to talk freely and to "unburden" themselves. Direct questions are avoided, and their results have been good. Psychological factors assume less importance if the offending allergen is found and removed.

Endocrine Factors.—Endocrine factors must also be considered, and the use of estrogens plus mild sedation is indicated for those with the "menopause syndrome." For those whose asthma is associated with menstruation, some relief is obtained by the use of ammonium chloride, with restriction of salt and water before menses.

Infections.—Infections sometimes help asthmatics; an attack of influenza, for example, may prevent asthmatic attacks for as long as six to eight weeks. The "common cold," however, frequently ushers in an attack, and many patients flatly state, "No colds, no asthma." The use of epinephrine in oil (see above) usually prevents asthma in such cases.

Mechanical Irritants.—Mechanical irritants are also to be avoided, especially dust, fumes, and smoke of all kinds. The recent Donora, Pa., disaster was a striking example. The people who lived in that valley were exposed to large amounts of noxious fumes, including gases and acids. Almost all who died or became seriously ill had either asthma or cardiac disease.

TREATMENT IN CHILDREN

The inheritance factor is very important in this disease. Spasmodic cough, colic, sniffles, or "eczema" frequently precedes the onset of the asthma itself. The asthma is usually paroxysmal, but chronic asthma can develop in children. Children rarely "outgrow" asthma.

The prognosis is better in children, and complications are less common. We prefer to do skin tests when the child is at least 9 months old. For asthma we use epinephrine or "sus-phrine," [6] aminophylline suppositories or rectally in solution, ipecac syrup, and potassium iodide, with or without ephedrine; morphine and other strong sedatives are avoided.

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10. Abramson, H. A.: Somatic and Psychiatric Treatment of Asthma, Baltimore, Williams & Wilkins Company, 1951.

The child's mental attitude should be as normal as possible. The child should not be pampered nor, on the other hand, allowed to be frightened because of the dyspnea. It is best to make a joke of the wheezing and explain that the "kittens are at it again." During attacks, exertion should be minimized, but between spells the child should go to school and play. The parents should not discuss the condition in the presence of the child. Most children take their injections as well as adults, often better.

TREATMENT OF ASTHMA IN THE OLDER AGE GROUP

In the older group with asthma, the reaction to skin tests are usually smaller, symptoms tend to be more chronic, and status asthmaticus, with its more serious prognosis, tends to be commoner.

Specific measures are as important as in younger life. Complete scratch and intradermal tests may turn up some unusual allergen, as in a man, aged 60, whose asthma was found due to karaya gum contained in material used to secure his upper denture.

In patients with negative reactions to skin tests we usually inject once or twice a week a mixture of extracts of house dust, feathers, and fungi in one arm and in the other small doses of a stock respiratory vaccine, and we continue to look for possible allergens. The homes of these patients are to be as dust-free as possible. We are not too enthusiastic about food allergy in this group, but, on the other hand, we continue to search for possible allergens and refuse to call these nonreactors hopeless.

It is necessary to keep up morale; to avoid infections, overwork, and exposure to irritant fumes; and to treat complications. The combined use of iodides and apomorphine hydrochloride (see above) is usually helpful, but one must be careful in using ephedrine and epinephrine because of possible slowing of urine output (men) and raising of blood pressure. Aminophylline, if given intravenously, should be injected very slowly.

The results in older patients are not good as in young patients but are at least as good as in any other branch of medicine and probably better. The outlook is rarely hopeless, even when complications exist. Warmer climates are often beneficial for those with chronic bronchitis and mild heart degeneration.

Elderly asthmatic patients can be placed into two groups, with distinct differences in treatment and prognosis. One group consists of patients who have had chronic allergic rhinitis and sinusitis, with or without polyps, or who have had many previous attacks of asthma. Results of skin tests are usually positive, complications are only as frequent as in nonallergic persons of similar ages, and the prognosis is rather good. In the other group, however, the asthma begins after the age of 40 to 45, with no previous allergic condition, and usually with negative or almost negative reactions to skin tests. The prognosis is less favorable, and complications are frequent, along with loss of strength, weight, and morale. Death is not infrequent, but, fortunately, the use of corticotropin and cortisone has greatly improved the prognosis in this group.

TREATMENT OF COMPLICATIONS

Asthmatic patients can have all sorts of complications, and treatment must be directed accordingly. For example, an asthmatic patient who needs a herniotomy or a cholecystectomy should first be placed in the hospital in a dust-free (asthma) room. When the asthma has subsided, the operation is carried out (ether anesthesia preferred), and the patient is returned to the "asthma" room. The asthma is kept under control so that postsurgical trouble is minimized, with less chance of recurrent hernia.

Emphysema.—Emphysema occurs in almost every case of chronic asthma and is easier to prevent than to cure. Unfortunately, therapy has not been too successful, although the following procedures have some value: (*a*) special breathing exercises, as recommended by the Asthma Research Council, London; (*b*) belts that elevate the diaphragm; (*c*) oxygen for cyanosis; (*d*) prolonged use of ephedrine, probably the best drug for emphysema; (*e*) care of associated infectious conditions, e. g., bronchitis; (*f*) pneumoperitoneum to raise the diaphragm; (*g*) removal to warmer climates, e. g., Arizona or around San Antonio; and (*h*) administration of corticotropin and cortisone, with increase in weight and morale.

Bronchiectasis.—Bronchiectasis occurs rather infrequently with bronchial asthma, probably more by coincidence than by cause and effect. Lobectomy is indicated for the saccular variety whenever it can be safely carried out, because all other measures, e. g., use of antibiotics, postural drainage, bronchoscopic aspirations, and instillations of iodized oil, give only temporary relief.

Sinusitis.—Sinusitis may be infectious or allergic (easily differentiated by the absence or presence of eosinophilia in nasal smears, fever, pain, and the like. The allergic variety requires the usual allergy measures, including administration of an antihistaminic drug. Infectious sinusitis usually responds to antibiotic treatment, although surgery is occasionally necessary.

Atelectasis.—Atelectasis, if massive, may be due to a mucous plug; the patient may cough up the plug with prompt relief, or bronchoscopic aspiration may be necessary. We have recently had good success in many patients by dissolving thick sputum by inhalations with "tryptar" (brand of purified cryptalline trypsin).[11]

The usual measures are indicated for other possible complications, e. g., spontaneous pneumothorax, subcutaneous emphysema, or a broken rib, and for such associated conditions as cardiac decompensation, pulmonary tuberculosis, diabetes, carcinoma, and hypertension.

COMMENT

The results depend to a large extent on (*a*) whether the asthma is paroxysmal or chronic and (*b*) the care given by the physician and the cooperation of the patient. The prognosis is much better in those who have the paroxysmal type with relief between spells. Those who have chronic asthma can also be benefited.[12]

11. Unger, L.: Letters of International Correspondence Society Allergists, 1952, series 15, p. 25.
12. Unger, L., and Wolf, A. A.: Treatment of Bronchial Asthma: Survey of Value of Treatment in 459 Cases During 20 Years, J. A. M. A. **121**: 325 (Jan. 30) 1943.

SUMMARY AND CONCLUSIONS

1. The term "bronchial asthma" should be restricted to the allergic condition that is characterized by generalized wheezing, dyspnea, orthopnea, and cough, usually associated with seasonal or perennial rhinitis.

2. The preventive treatment is important in children of allergic parents. Ten suggestions are given.

3. Best results come from specific measures: elimination of the offending allergens and hyposensitization with extracts of important allergens that cannot be sufficiently avoided. These methods of treatment are outlined.

4. Symptomatic measures are discussed as necessary for attacks at home and in the hospital and for periods between spells. Special reference is made to reassurance of the patient, to such drugs as epinephrine, aminophylline, ephedrine, and iodides, and to bronchoscopic aspirations and antibiotics.

5. Sedation should be as mild as possible; antihistaminic drugs, phenobarbital, and alcohol are recommended. The use of morphine, meperidine hydrochloride, and strong hypnotics is to be avoided.

6. Corticotropin (ACTH) and cortisone are valuable in the treatment of status asthmaticus that has resisted the usual therapy. They should not replace agents the use of which is based on a thorough allergy survey.

7. Psychological factors must be dealt with but become less important if the offending allergen is discovered and can be avoided.

8. Treatment is outlined for asthma in children and in the older age groups, and for complications.

9. Results of treatment are excellent in patients with paroxysmal asthma but are less favorable in patients with chronic emphysema.

185 N. Wabash (1).

PSYCHODYNAMIC PHARMACOLOGY OF THE TREATMENT OF ASTHMA

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Corticotropin (ACTH), cortisone, and related substances are now generally used in the treatment of the allergic state. Because of their striking effects on the psyche,[1] it appears desirable to recall that not only these substances but also other drugs in common use produce emotional changes in the allergic patient. It becomes more incumbent on the general physician, therefore, to become acquainted with the adaptive mechanisms of the personality structure of the asthmatic patient. In this way the pharmacologic response to therapeutic agents may be interpreted and often predicted in terms of the emotional state of the patient.

If cases of obvious chemical and physical causation are omitted, the cause of bronchial asthma is basically immunologic in nature. However, the intensity and persistence of asthma is maintained in an appreciable number of patients because of the presence of unconscious conflicts that lead to difficulties in the conscious, realistic realm of day by day activities. The nature of these conflicts in asthmatic persons has been in part determined by psychoanalysis. While it is essential for the general physician to understand the relationship of unconscious conflicts to the origin of asthma, this should not be used directly in therapy.[2] Indeed, the material obtained by psychoanalysis should not ordinarily be the subject of direct discussion between physician and patient.

An analogy will illustrate what is meant by the unconscious. There are in New York City two methods of projecting motion pictures. The type most commonly used is that in which the light is passed over the heads of the audience onto a reflecting screen. Portrayed on the screen is a realistic pattern of activity readily observed by the audience. The origin of this pattern is easily traced back to the projector that throws these realistic images on the screen. These images on the screen correspond to the clinical manifestations of the patients which are accessible and observable. The second type of motion picture projection is commonly found in newsreel theaters. In this type, the same activity is readily visible on the screen but there is no orienting beam of light to be traced back to the projector. The screen in this case is both reflecting and transparent. The projector is invisible and is situated behind the screen. There is no way of immediately deriving, from the realistic activities on the screen, the hidden mechanisms embodied behind the screen in the projector. The unconscious mechanisms of the patient are just as hidden from the physician, perhaps more so, than the projector in the newsreel theaters where the projector and the sound track are behind a screen and not available to the observer of the screen except by passing to the area behind the screen. The procedure of psychoanalysis elicits unconscious material by determining in part the psychodynamic mechanisms that result in realistic activities observable by the physician. Although it is necessary to recognize that mechanisms behind the screen of conscious activities of the patient determine his symptoms and complaints, it is usually difficult to utilize them directly in the treatment of the acutely ill asthmatic patient. The physician should be more concerned with recognizing the general psychological pattern by means of which he deals with his inner stresses, in conjunction with utilizing the action of drugs in an explicit relationship to the immediate, dominant emo-

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1. Rome, H. P., and Braceland, F. J.: Psychological Response to Corticotropin, Cortisone, and Related Steroic Substances: Psychotic Reaction Types, J. A. M. A. **148**: 27 (Jan. 5) 1952. Brody, S.: Psychiatric Observations in Patients Tested with Cortisone and ACTH, Psychosom. Med. **14**: 94, 1952.

2. The responsibility of the general physician in this area of medical practice was recently well expressed by Terhune, who stated, "Just as soma and psyche are aspects of one personality, physiologic and psychologic treatment are complementary; the family doctor should administer both simultaneously. To understand and treat a patient, the physician must know not merely the individual's physical condition, but also his psychologic make-up, his habitual patterns of reaction and the psychodynamics of his behavior, particularly those which may motivate his present illness." Terhune, W. B.: Integration of Psychiatry and Medicine: An Orientation for Physicians, New York, Grune & Stratton, Inc., 1951, p. 50.

tional state of the patient. It is necessary, therefore, to recognize and to utilize the psychodynamic pharmacology of drugs like epinephrine, the barbiturates, ephedrine, the carbromals, and narcotics, used in the treatment of asthma.

It was first shown by Eduardo Weiss [3] and by French and Alexander,[4] and later by others, that the outstanding psychodynamic process in the asthmatic patient is the unconscious fear of the loss of the mother or mother substitute. These unconscious psychomotive forces, developed in early childhood, are modified and diverted by the psychological, physical, and cultural growth of the patient, with this fundamental and unconscious pattern of anxiety, however, persisting. The intensity of other psychomotive forces may change the syndrome observed in asthma so that the patient almost always presents a mixed syndrome with certain features outstanding. In the following schematic classification the dominant emotional pattern that the asthmatic patient exhibits is taken as a guide to therapy, and pharmacologic measures should be initially adapted to the impression gained after study of the patient as a whole. Often administration of the drug will intensify the neurotic pattern, so well demonstrated by results of the administration of cortisone, and thus confirm the diagnosis by increasing the severity of the symptoms. With this concept in mind, some additional aspects of psychodynamic pharmacology of the therapy of asthma will be outlined.

PSYCHOLOGICAL TYPES OF PATIENTS

The general psychological types of asthmatic patients are classified here for purposes of therapy as follows: (1) the anxious asthmatic patient, (2) the depressed asthmatic patient, (3) the grieving asthmatic patient, (4) the hostile asthmatic patient, (5) the dependent asthmatic patient, (6) the euphoroid asthmatic patient, and (7) the phobic asthmatic patient.

The Anxious Asthmatic Patient.—An undercurrent of anxiety characteristic of chronic disease is especially prominent in all cases of bronchial asthma. Interference with breathing is always a threat to life. This is well emphasized by the frequent occurrence of psychoneuroses after minor gas injuries, especially noted in World War I and in industrial accidents at the present time. Another instance that illustrates the special attitude toward lung injuries is the attitude of volunteers in World War II toward experimental production of mustard burns. Volunteers were readily obtained for experimental skin lesions, but great reluctance was encountered when inhalation experiments were suggested even though reassurance was given that no permanent injury would result.[5] This undercurrent of anxiety may become a dangerous undertow in the asthmatic patient. The danger lies not only in the immunologic and psychologic realms but also in overtreatment by the physician. Indeed, it is well recognized among allergists that many patients with bronchial asthma are subjected to pharmacologic trauma, when the drug intensifies the symptoms because of the mental state of the patient.

If one accepts the point of view that an undercurrent of anxiety exists, practically speaking, in all cases of asthma, it is important to search for symptoms connected with anxiety. For example, in taking the history it is necessary that one ascertain whether the asthmatic attacks started by difficulty on inspiration or difficulty on expiration. The respiratory cycle, in many cases, must be carefully explained to the patient. However, after the patient understands the respiratory cycle, instead of saying that the attack was asthma, he may say that there was difficulty in getting air or in catching the breath. Difficulty in catching the breath or in getting the breath is not equivalent to a classical attack of asthma. In classical asthma of course, the difficulty is on expiration. If there is difficulty on inspiration, and especially if the attack of asthma begins with difficulty on inspiration, it is wise to administer, in very small doses, epinephrine by injection or inhalation, or ephedrine and related substances orally. This is necessary because epinephrine itself is likely to produce anxiety if given in larger doses. Often difficulty on inspiration develops in a mixed syndrome, with difficulty on expiration dominating the picture. The underlying anxiety is just as important a part of the pattern that has to be treated as the difficulty on expiration, which under ordinary circumstances responds to treatment with the sympathomimetic amines.

Another aid in determining the degree of anxiety is observation of the patient's oxygenation. If the action of chest muscles is great and the color is good, it may be desirable to use oxygen, with the understanding that the response to oxygen in a case of this type may be more of a test for an underlying neurosis than an active therapeutic procedure embodying pharmacologic action. Patients of this type often respond almost immediately to oxygen therapy. Indeed, frequently a patient claims relief within one minute after having the tube, with oxygen passing through it, placed in the mouth. Sometimes, relaxation follows merely placing the tube in the mouth, even before the oxygen starts to flow. Anxious patients may often refuse to go into the tent or wear an oxygen mask. This anxiety is important, because it reflects a phobic component in the patient's make-up. The use of sedation in patients with anxiety is usually indicated. The use of chloral hydrate, with or without the barbiturates, is effective. There is no routine dosage. The dosage depends on the pharmacologic response of the patient as well as his character structure. This is of importance in certain patients in whom sedation leads to regression to an infantile level, thus decreasing the cooperation and increasing the infantile behavior. The predominantly anxious type will often speak of dying during the attack. Reassurance is desirable, even if the patient himself does not suggest the possibility of death. It is always wise to make certain that the patient understands that asthma is a chronic disease that can be prevented from becoming serious if he cooperates with the physician.

Case 1.—A 58-year-old man having severe asthma as a complication of an upper respiratory tract infection was given 5 grains (0.30 gm.) of chloral hydrate four times per day. He was ill enough to be confined to bed. On one occasion when I was present, and the patient was under the influence of chloral hydrate, he called, "Mamma, Mamma." His wife, who was always

3. Weiss, E.: Psychoanalyse eines Falles von nervoesen Asthma, Internat. Ztschr. f. Psychoanal. v. Imago 8: 440, 1942.

4. French, T. M., and Alexander, F.: Psychogenic Factors in Bronchial Asthma, Psychosomatic Medicine Monographic Series, no. 4, 1941.

5. Abramson, H. A.: Unpublished observations made at Edgewood Arsenal and Suffield, Canada, 1943-1945.

called Mamma by the patient, ran in and said, "Papa, what do you want?" He said, "I don't want you, I want my own Mamma." This statement was most dramatic. The conditions under which this patient was observed permitted the entrance into a conscious level of a fundamental anxiety under the influence of sedation. The patient had also regressed into an infantile level in other ways. He was petulant, complaining, and coercive. He demanded constant attention in minor matters during his period of illness. His wife, fortunately, was reasonably solicitous and adapted herself well to this maternal role. In this case, the deep urgency during an asthmatic attack to be cared for by his own mother, long since dead, manifested itself by direct expression under sedation.

The Depressed Asthmatic Patient.—This type of patient is often found to be submissive and obedient, which is a reflection of his depressed attitude. Therefore, one should note carefully the effect of sedation, which may be contraindicated. The depressed patient often prefers epinephrine by injection rather than by inhalation because of the stimulating effect of the injected epinephrine. The patient feels better, but the vital capacity may remain unchanged. The depression should be treated cautiously by the administration of amphetamine sulfate, after breakfast and after lunch. Even though amphetamine is taken by mouth, epinephrine as an aerosol is not contraindicated, nor are small doses of sedative in the evening and at bedtime. An extreme example of a depressed patient is one who greets the physician with the statement "No one can help me. I have been treated by many doctors and I am still sick." It is important to recognize that these patients do not respond to ordinary therapy. Intensive psychotherapy, if acceptable to the patient, may be indicated. Chemical hypnosis for the patient who states the equivalent of "no one can help me," might be a desirable procedure in order to elicit rapidly the basis of the patient's desire to retain a negativistic attitude toward therapy.

CASE 2.—It was noted that a 40-year-old married woman with two children, while hospitalized for status asthmaticus, did not improve sufficiently in view of the absence of a pathological condition. She requested frequent injections of epinephrine, after which she felt better. It was also observed that her breath sounds did not appreciably change after the use of epinephrine, with her breathing difficulty essentially the same. It was concluded, therefore, that this patient was depending on epinephrine injections, not for relief of her bronchial spasm, but for the stimulation of the central nervous system. Therapy with dextro-amphetamine sulfate was begun with 2.5 mg. administered twice a day during breakfast and lunch. On the addition of amphetamine to her therapeutic regimen there was immediate and rapid improvement with loss of the depressed state manifesting itself sharply. This patient eventually was able to take as much as 10 mg. of amphetamine at one time in addition to using epinephrine aerosol (glycerinated).

A depressed state in a patient may also be brought on by therapy. In the following case the iatrogenic agent was cortisone.

CASE 3.—A 64-year-old woman was hospitalized with the chief complaint of difficulty in breathing for three weeks. Her illness began five years before admission. After a family quarrel with her daughter she experienced tightness in the chest and shortness of breath. In addition, there was wheezing and dyspnea, both of which responded to routine treatment for asthma. There had been fluctuations in the severity of her symptoms, with the severe symptoms usually responding to medication. Apparently the present attack of asthma followed an upper respiratory tract infection complicated by bronchitis. In the three weeks she had lost 20 lb. (9 kg.). Her vital capacity on admission was 1,000 cc. The patient voluntarily traced her onset of asthma to her husband's prostatectomy, five years before. She was irritable, hostile, and resentful of her lot in life. After she had received 1,600 mg. of cortisone, the vital capacity remained unchanged but she became depressed and comparatively unmanageable. She decided to leave the hospital because of the deterioration of her condition. It was of interest that, after the cortisone therapy was stopped, prior to her leaving, with the improvement in mood following the withdrawal of the drug, her difficulty in breathing was improved although her vital capacity remained unchanged.

The Grieving Asthmatic Patient.—Such a patient is an unhappy person who is in all likelihood substituting the asthmatic attack for what may be an unrecognized feeling of grief. The patient presents a syndrome often mixed with dependence and depression. This may be observed in pollen-sensitive patients whose pollen asthma is prolonged without suitable reason into the winter months. It is important to recognize the grieving asthmatic patient and to make certain that the physioligical needs of the patient are taken care of with suitable reassurance and minimal use of sedatives and of the sympathomimetic amines. Breathing exercises accompanied by an expiratory hum or moan may be prescribed hourly. The expiratory hum aids the patient apparently to express as a cry the unconscious anxiety mentioned. Indeed, the expiratory hum may prevent an attack of asthma.

CASE 4.—The grieving asthmatic patient often, for reasons of his own, masks his grief. This syndrome may be relieved by the patient's expressing grief uninhibitedly. A young woman, 24 years old, who was planning to get married and leave her parents' home for the first time, was first seen in status asthmaticus. The attack had been initiated by ragweed pollen at the onset of the pollen season but continued on through the winter, far beyond the pollen season. All the measures usually effective in interrupting status asthmaticus were employed by her regular physicians without any result. When I first saw her, the patient had good color but at the same time had extreme difficulty in breathing. The clinical impression made by the patient was important. She was the picture of grief, vainly asking for help during a severe asthmatic attack, but none of the help really desired, i. e., recognition of her grief, had been offered. I asked her whether she wanted to cry. She said, "Should I cry Doctor?" She was told, "Try." During this time the conversation was maintained without difficulty by the patient for a few minutes, during which she was reassured that crying would be good for her. She was given 5 grains (0.30 gm.) of chloral hydrate in warm water, which she sipped slowly. After several minutes of discussion she burst into tears and cried for 15 minutes with deep, gasping sobs; she then relaxed on her pillow with definitely diminished asthmatic breathing. Indeed, she was well enough to leave the hospital in three days.

CASE 5.—A young woman, clinically sensitive to a variety of inhalants and foods, lost her usual response to ephedrine and epinephrine therapy. She was told to perform a breathing exercise that is a definite type of psychotherapy as well as physical therapy. The patient is instructed to extend the hands forward while inhaling. On exhalation the hands are brought to the side, but during expiration the expiratory breath is made slowly and a humming, crying sound is made through the closed lips. It is interesting to see the reaction of patients when this exercise is demonstrated. The crying sound, of course, has many implications, and most patients smile in an embarrassed way. However, this patient readily utilized this type of exercise when she felt an attack coming on. She was advised to breathe in this way one to two minutes every hour on the hour during her period of tension and difficulty in controlling the wheezing in her chest. She improved considerably. As a matter of fact, she was finally able to use this exercise in the subway when she felt heaviness in the chest by merely thinking of the movements and of the crying expiratory whimper that she had been instructed to carry out.

The Hostile Asthmatic Patient.—This type of patient in contrast to the preceding one, frequently camouflages his attitudes by apparently cooperating fully with the physician. The sympathomimetic amines, either by injection or aerosols, should be used with caution. In this type, sedation is often effective and regression to an infantile level because of the sedatives is not frequent. Patients of this type can frequently take 0.2 gm. of amobarbital (amytal®) sodium four or five times daily and still function fairly well under hospital conditions.

The Dependent Asthmatic Patient.—Certain patients showing anxiety, especially children, may make neurotic utilization of their asthma in order to obtain attention from a parent or parent figure. In the young child, the conscious and the unconscious are not as clearly defined as in the adult. Utilization of asthma is often frankly admitted by the child. It is frequently necessary to separate the child from the parents, even though the fear of the loss of the parent's love is the basic anxiety. Of course, a suitable mother substitute must be provided. Dr. M. Murray Peshkin's pioneer studies on this subject are pertinent.[6] They show conclusively that the fear of losing the parent's love when actually realized in a threatening parental home can be readily controlled by removal of the asthmatic child to an accepting warm emotional climate even though the environment is an institution with parent substitutes. In the adult the dependence on the parent or on the husband or wife playing the role of the parent figure should be observed, noted, and utilized in therapy. Treatment of these patients should include in the home a routine in which constant reassurance and support is given. Treatment with moderate sedation and small doses of sympathomimetic amines, by any route, is indicated.

CASE 6.—A 10-year-old girl, who had severe asthma for many years, was treated by injections of specific vaccines and by antihistaminic aerosols as well as by being sent out of town to the home of her grandmother. None of these measures was effective. Contrary to my advice and that of the pediatrician, she was sent to a school far removed from the influence of her parents and siblings in a region where allergens to which she was allergic were present. There was immediate improvement in the asthma, and she gained approximately 15 lb. (6.8 kg.) in the school year.

This is an example of a case in which separation of a child from mother, father, and siblings solved many immediate but unknown emotional problems. This is confirmatory of the view of Peshkin, who speaks of "parentectomy" as a necessary major procedure in certain cases of intractable asthma in children.

The Euphoroid Asthmatic Patient.—A certain number of asthmatic patients have developed an adaptive mechanism that requires that they consider themselves well and healthy persons. This is found especially in young persons, I believe, who fear yielding to the consequences of their unconscious wishes to be dependent. They react by using their mechanisms of adaptation to subordinate their asthmatic condition to their need for recognition as independent persons. Patients in this group often come into the physician's office and carefully avoid mentioning that they have had asthma and refer to their chief complaint as hay fever. This type of patient, unlike the depressed patient, says, "I do not really need your help." Only adroit questioning by the physician will bring out the severity of their symptoms. This is often made possible in young active men who have large vital capacities. Thus, a young male patient being treated for hay fever was given a physical examination, and typical asthmatic breathing through the chest was heard. He denied that he had any asthma and proceeded to prove it by having a vital capacity of 4.6 liters. However, this young man's chest (his weight was 135 lb. [61.2 kg.]) was unusual in its configuration, so that his vital capacity was above normal. After treatment with epinephrine aerosol, his vital capacity rose to 5.8 liters and his asthmatic breathing disappeared.

Another illustrative case of a euphoroid state is that of a 30-year-old business man, who claimed that he had some asthma but that it had not interfered with him or his work except on three occasions during the year, when he had serious attacks. Frequent studies of his vital capacity carried out throughout weeks revealed that his feeling of well-being masked a rather serious asthmatic syndrome, which kept his vital capacity at 50% of normal for most of the time. So anxious was he to appear well that he would go skiing in the midst of an asthmatic attack, thereby supporting his euphoroid conclusion that he was well.

This type of euphoroid state in a sense is self-destructive and probably represents the patient's way of dealing with unconscious hostility that he is incapable of mastering. The scratching eczema patient thus often turns his aggression on himself. The euphoroid asthmatic patient, by abusing his respiratory system, receives the love and affection that he needs from his family as a secondary form of reassurance that they do not recognize his own hostile feelings toward them. Psychotherapy is indicated for this type of personality, who will, so to speak, deliberately endanger his life by denying the existence of a chronic disabling disease.

CASE 7.—The spectacular development of euphoria in patients with asthma is well illustrated by the behavior of a 30-year-old asthmatic man who had recovered from asthma temporarily after treatment with cortisone. The patient, who had responded to none of the conventional methods of treatment, was presented at a recent clinical conference of 150 physicians. He willingly walked up to the microphone and told a somewhat astounded group what a miraculous drug cortisone was. It was with some difficulty that he could be separated from the microphone and again play the role of patient. In this instance the patient's recovery corresponded with reality to a certain degree, in that his pulmonary difficulty improved.

In the following case the patient's recovery was more on the psychological side.

CASE 8.—A 28-year-old laborer had had severe asthma for many months complicated by bronchiectasis and eczema. He had been treated unsuccessfully for his bronchiectasis, which was of many years' duration, and coughed up approximately 100 cc. of mucopurulent material daily. On hospitalization he showed definite paranoid tendencies. Attempts were made to improve his bronchiectasis by treatment with penicillin aerosols, which he, for some unknown reason, refused to continue. On treatment with cortisone euphoria developed, the asthma improved slightly, and he stated, "I have never felt better in my life; my skin is like a baby's." However, the physical signs and roentgenogram of the chest remained unchanged. There was only moderate improvement in the skin, and he also still coughed up approximately the same volume of mucopurulent material.

6. Peshkin, M. M.: Report presented at the Fortieth Anniversary Convention, National Home for Jewish Children, September, 1947.

It is possible that the maintenance of the euphoric state in this patient might lead to better appetite and improvement similar to that which occurs during treatment of tuberculosis with isonicotinic acid hydrazids.

The Phobic Asthmatic Patient.—The phobic asthmatic patient, although not so common a type, complains mainly of difficulty in breathing with a feeling of constriction of the chest accompanied by a minimal quantity or absence of wheezing, with poor vital capacity but good breath sounds and no emphysema. He may be afraid of the street. Many fears, such as claustrophobia and fear of elevators, crowds, street cars, and busses, restrict his activities. These phobic problems are fundamentally emotional and should be handled as such.

SPECIAL PROBLEMS IN CURRENT THERAPY

Pollen Therapy.—The administration of pollen extract is, in general, not attended by any acute danger or repeated injury to the patient. However, Castberg and Schwartz have demonstrated that in young patients with hay fever, after administration of shocking doses of pollen extract, important changes occurred in the electrocardiogram.[7] In all cases, changes typical for anoxemia of the myocardium were found. This raises many questions. What, for example, is the effect of overdosage over prolonged periods, for many years? Do the doses producing subclinical shock in the tissues lead to chronic changes due to therapy? To avoid overdosage, the local reaction of the patient's skin during therapy as well as general reactions are the guide to therapy, rather than any particular number of units advocated for a given patient in a routine fashion. The psychological implications in the administration of subanaphylactic doses include a threat to the patient of anaphylactic shock and its consequences. This is unwarranted by any increased value in therapeutic result attained. Small doses without the dangers of anaphylaxis have in my experience provided adequate protection.[8] The above notations on pollen extract apply equally to other specific allergenic extracts and nonspecific preparations.

Antihistaminic Drugs.—With few exceptions, antihistaminic drugs have, aside from their effects on the pharmacologic action of histamine, one definite characteristic in common: their hypnotic effect. In addition, there is also a definite atropine-like effect, which accounts for the drying of the mucous membranes in the therapy of hay fever; because of this, they should be used with caution in patients with asthma, especially when associated with bronchial infection. When physicians prescribe antihistaminic drugs for allergic disorders, are they prescribing these drugs to counteract the effect of histamine or prescribing them for the hypnotic and atropine-like action combined with a decrease in the permeability of the small blood vessels? When the antihistaminic drugs are effective in asthma, it should be borne in mind that they may be so because of a hypnotic effect rather than an antihistaminic effect. In the presence of anxiety, the hypnotic effect of the antihistaminic group is often observed. The combined pharmacologic action of these depressants with ordinary sedatives is unpredictable on the basis of available data.

It is necessary to recall that there are other drugs that are more truly antihistaminic in their pharmacologic action. Notable among these is epinephrine. The antihistaminic effect of epinephrine and related drugs is many times greater than that of any antihistaminic drug. In addition to having an antihistamine effect, epinephrine also shows the restoration effect. That is, many hours after epinephrine neutralizes histamine in the skin by vasoconstriction (a true pharmacologic antagonism) the epinephrine again may manifest itself by vasoconstriction at the site of histamine action.[9] Similar general reactions were observed first by Cameron,[10] who found that histamine neutralized the general effect of epinephrine only in a transient fashion. These observations make unlikely the theory that epinephrine liberates histamine in a quantity of clinical significance.

Epinephrine.—One of the most useful methods of treating asthma is by the nebulization of a 1:100 epinephrine salt solution, provided that certain conditions are fulfilled[11]: 1. The droplets are stable and do not evaporate rapidly. 2. Therapeutically suitable particle size distribution is achieved. 3. Nebulizer delivery is adequate.

Once the nebulizer has been chosen, it is important that the nebulizer operate efficiently with the solution employed. The important feature of all of the solutions is the fact that they contain about 1% biologically active epinephrine.

Failure with this type of therapy may usually be traced to (1) insufficient solution being used in the nebulizer, (2) a poorly constructed nebulizer, (3) insufficient glycerin or other stabilizing substance, (4) an excessive amount of secretion in the bronchial tubes, preventing access of the aerosol to the points required, or (5) an emotional state of the patient, e. g., anxiety, in which the sympathomimetic amines are essentially contraindicated except in very small doses.

Often patients in an anxiety state are called "epinephrine fast." The so-called "epinephrine fastness" of these patients is not always due to the fact that epinephrine has been employed. Indeed, "epinephrine fastness" can be observed to occur in several categories: (1) when epinephrine has not been used for some time, (2) when only a small amount of epinephrine has been administered, and (3) when a considerable amount has been administered. In view of the fact that "epinephrine fastness" can occur when there has been no opportunity for a true pharmacologic tolerance to be achieved as under categories (1) and (2), it is important that the emotional state of the patient be considered. Epinephrine should never be administered if it is not obviously effective. If epinephrine derivatives given by mouth are not satisfactory, the patient should be instructed to use epinephrine aerosol whenever possible to prevent an impending attack. In this way, the excellent results obtained with epi-

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7. Castberg, T., and Schwartz, M.: Changes in Electrocardiogram During Allergic Shock, Acta med. scandinav. **126**: 459, 1947.

8. Abramson, H. A.; Loebl, M.; Gettner, H. H., and Sklarofsky, B.: Therapy of Ragweed Hay Fever with Electrophoretically Isolated Fractions (Artefolin and Trifidin): Preliminary Report, Ann. Allergy **8**: 594, 1950.

9. Abramson, H. A., and Grosberg, S.: Skin Reactions: Comparison of Antihistaminic Action of Pyribenzamine and Epinephrine Introduced into the Human Skin by Electrophoresis, Ann. Allergy **7**: 325, 1949.

10. Cameron, D. E.: Increased Reactivity Caused by Adrenalin, Am. J. M. Sc. **213**: 331, 1947; Adrenalin Administration in Persistent Anxiety States, ibid. **210**: 281, 1945.

11. Abramson, H. A.: Principles and Practice of Aerosol Therapy of the Lungs and Bronchi, Ann. Allergy **4**: 440, 1946.

nephrine aerosol therapy justify the statement that in most instances inhalation can replace injection.

Barbiturates and Acetyl Carbromal.—The dangers inherent in the unrestricted use of barbiturates are perhaps overemphasized by the following case; nevertheless, results in this case remind one to be judicious in the administration of these compounds.

CASE 9.—A 27-year-old asthmatic woman had emotional problems that were obviously connected with the presence of many immature traits. After taking one capsule of pentobarbital sodium, she proceeded to take the remainder in the box—about five capsules. Fortunately, this was observed by her husband, who was able to get her to vomit the capsules. This was repeated on a subsequent occasion, when pentobarbital sodium was again administered. It is not known whether this patient was specifically stimulated by pentobarbital sodium, but it is of interest that in her family barbiturates have unusual effects, leading to suicidal drives. She was able to take chloral hydrate for sedation without difficulty.

It is common to employ ephedrine sulfate, ⅜ grain (25 mg.), with some barbiturate like secobarbital, pentobarbital, amobarbital, or phenobarbital sodium to counteract the effect of ephedrine while bronchodilatation is induced. The use of barbiturates in patients with a chronic illness is often contraindicated. Indeed, the increasing employment of barbiturates lends emphasis to the growing need for the use of mild sedation in the therapy of asthma, in which barbiturates can be dispensed with. During the past year I have employed acetyl carbromal (sedamyl®), 0.25 gm., combined with ephedrine sulfate 25 mg., one capsule being given at the onset of an asthmatic paroxysm.

This combination has been found superior to standard combinations of ephedrine with phenobarbital, in which ¼ grain (15 mg.) of phenobarbital was present to counteract the effect of ephedrine. It apparently may equal barbiturate-ephedrine mixtures in efficiency, producing a suitable response to the ephedrine without producing the toxic symptoms of nervousness after the use of ephedrine alone. Further investigation may show that 4 grains (0.26 gm.) of acetyl carbromal may effectively take the place in many instances of the barbiturates when combined with ephedrine in the therapy of asthma. This sedative may be a most useful addition to the therapy of asthma because of the possibility of avoiding the growing tendency toward barbiturate addiction.

Narcotics.—There does not seem to be much disagreement with the opinion that morphine is contraindicated in patients with asthma, not only because of its depressant effect and the probability of habituation but also because morphine often causes death, especially in patients in middle life. Related drugs like meperidine hydrochloride are also respiratory depressants and are definitely habit forming. The anxious patient who requires quieting can be treated by ways other than those provided by habit-forming narcotics. If the therapy of asthma depends on the use of habit-forming narcotics, then psychotherapy is indicated.

Cortisone and Corticotropin.—These drugs have been reviewed extensively in the references given. Perhaps it is well to emphasize what Rome and Braceland [1] pointed out: 1. Psychotic reactions are complications to be expected. Further, patients with various allergic disorders are more susceptible to the development of psychiatric complications than other persons. 2. Induced hypercorticalism mobilizes physiological and psychological sources that upset the dynamic equilibrium of the adapting state of the patient. It is necessary, therefore, for the clinician to be acquainted with the component adaptive capacity of the patient he is treating. This point of view is illustrated in the cases reported here.

COMMENT

In presenting this paper I have tried to stress the practical considerations of the somatic and psychiatric treatment of asthma with the hope of stimulating thought to the treatment of the patient, not the asthma alone. Combined attention to organ and person always produces better therapeutic results than exclusive attention to the diseased organ. How can this be achieved? In the final analysis the large majority of the psychologically disturbed patients are expected to remain with the general physician. This gives him the responsibility of having a good working knowledge of psychiatry. This goal is not difficult to achieve.

SUMMARY

While it is generally agreed that therapy should not neglect the physiological and the immunologic condition of the patient in the asthmatic state, the physician should not ignore the personality of the patient in planning suitable therapeutic procedures. It is neither wise nor desirable for the patient with severe asthma to be reminded of unconscious material that the physician himself may be aware of. It is more than desirable in our present state of knowledge to use pharmacologically active drugs in connection with the total personality of the patient manifested during the acute asthmatic attack. Whether anxiety, phobia, depression, dependence, hostility, grief, euphoria, or other pattern dominates the asthmatic attack, the physician should bring into the proper sphere the psychodynamic pharmacology of the drug employed in treating both the asthmatic spasm and the personality of the patient himself. In this way a better understanding of the action of the drugs on the personality of the patient will be obtained, with much greater predictability in the therapy of bronchial asthma.

133 E. 58th St. (22)

Antibacterial Therapy of Tuberculosis.—Antimicrobial agents have become indispensable in the treatment of tuberculosis, but should be combined with other appropriate forms of treatment such as rest, collapse therapy, and surgical procedures. The best regimen available today for most patients with tuberculosis is the combination of 1 gm. of streptomycin or dihydrostreptomycin given intramuscularly two or three times each week plus 12 gm. of PAS given orally, each day. The optimal duration of therapy with streptomycin and PAS is not known. At least 6 to 12 months of therapy seems advisable; patients with the more serious manifestations of tuberculosis should be treated 18 to 24 months or longer.

Preliminary studies suggest that isoniazid and its isopropyl derivatives are potent antituberculosis agents, particularly valuable in the treatment of patients with tubercle bacilli which are highly resistant to streptomycin. Further studies are needed to determine their proper use in these cases and also in patients with streptomycin-susceptible tubercle bacilli. There is no evidence that either of these drugs is as effective as the combination of streptomycin and PAS.—Committee on Therapy, American Trudeau Society, Developments in Antimicrobial Therapy of Tuberculosis, *American Review of Tuberculosis*, August, 1952.

ADRENAL VIRILISM

I. DIAGNOSTIC CONSIDERATIONS AND TREATMENT

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The virilizing syndrome in children is characterized by the masculinization of the female and the attainment of precocious puberty in the male. There are some variations in the clinical syndrome that depend on the age of onset of the disease and the endocrine gland responsible. In the female, infantile virilism presents the clinical picture of pseudohermaphroditism and subsequent early masculinization. If the disease has its onset later in childhood, there is superimposed masculinization of the normal female genitalia. In the male, on the other hand, the precocity is along isosexual lines with the resultant clinical picture of macrogenitosomia precox.

The virilizing syndrome may be associated with hypothalamic disease, constitutional precocity (both of which occur in boys along isosexual lines), and testicular or ovarian tumors, and, most frequently of all, may be due to hyperadrenalism. Because of this commoner occurrence, the syndrome has been called "adrenal virilism."

Adrenal virilism may be caused by adrenal hyperplasia, adenoma, or carcinoma. The latter two conditions are amenable to surgery, and, if neoplasms are completely removed, the progress of the disease can be arrested.[1] The treatment of adrenal hyperplasia, until recently, has been extremely discouraging to the distressed family and to the therapist. Subtotal adrenal resection has been performed without consistent benefit. Large doses and prolonged administration of estrogens have been employed in an attempt to overcome the excessive androgen effect. This regimen was of some benefit in the behavior problems but produced the effects of excessive estrogen therapy without reduction of the androgen effect. As a whole both the operative and estrogen effects have not been very successful.

In this syndrome, the determination of the urinary 17-ketosteroids is of great diagnostic importance, since it is devoid of metabolic disturbances in the electrolyte, carbohydrate, and protein spheres. Invariably, adrenal virilism is accompanied by increased values of the 17-ketosteroids in excess of five to ten times the normal values for children under the age of 10, which are between 1 and 3 mg. per day. Adrenal carcinoma has been associated with excessive urinary excretion of the β-ketosteroids or dehydroisoandrosterone.[2] Curiously enough the excretion of estrogens in virilism may be high as well without recognizable effect on the patient.[3]

Recently, several reports have appeared in the literature that indicate that cortisone therapy may be effective in controlling adrenal virilism due to cortical hyperplasia.[4] The administration of cortisone to these patients results in a dramatic fall in the urinary 17-ketosteroids and estrogens to approximate normal values. It has been postulated by the three groups of investigators [4] that cortisone has its effect by inhibiting endogenous corticotropin (ACTH) secretion by the patient's own pituitary, resulting in a decreased secretion by the adrenals. The purpose of this report is to present in detail experience with the use of cortisone and compound F on 17 patients with the virilizing syndrome and to recommend a program of diagnosis and treatment based on such a study.

METHODS AND MATERIALS

Of the 17 patients studied in this series, 14 were confined to the wards of either Babies Hospital or the Presbyterian Hospital, where the collection of urine specimens could be adequately supervised. One patient was studied at St. Luke's Hospital. In the younger children, indwelling catheters were inserted in order to insure complete urine collections. After suitable control periods of two to seven days (which of necessity were of short duration in the catheterized patients) 25 to 200 mg. of cortisone per day, intramuscularly or by mouth, was administered to 15 patients, and 100 to 200 mg. of compound F was injected daily in 2 for varying lengths of time. Urinary 17-ketosteroid determinations were performed by the Zimmerman reaction as modified by Holtorff and Koch.[5]

Seven of the patients studied were first given 75 to 100 mg. per day of corticotropin in an attempt to ascertain whether these hyperplastic adrenal cortexes could be further stimulated. After this period, cortisone was administered. Of the remaining 10 patients, 8 received cortisone and 2 compound F.

Damon Runyon Senior Clinical Research Fellow (Dr. Jailer); Squibb Fellow in Endocrinology (Dr. Louchart).

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Cortisone and compound F used in this study were supplied by Merck, Inc., and the corticotropin (ACTH) by Armour Laboratories.

From the Departments of Medicine, Obstetrics and Gynecology, and Urology, College of Physicians and Surgeons, Columbia University and the Presbyterian Hospital.

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2. (*a*) Talbot, N. B.; Butler, A. M., and MacLachlan, F. A.: Alpha and Beta Neutral Ketosteroids (Androgens): Preliminary Observations on Their Normal Urinary Excretion and Clinical Usefulness of Their Assay in Differential Diagnosis, New England J. Med. **223**: 369, 1940. (*b*) Allen, W. M.; Hayward, S. J., and Pinto, A.: A Color Test for Dehydroisoandrosterone and Closely Related Steroids, of Use in the Diagnosis of Adrenocortical Tumors, J. Clin. Endocrinol. **10**: 54, 1950.

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5. Holtorff, A. F., and Koch, F. C.: The Colorimetric Estimation of 17-Ketosteroids and Their Application to Urine Extracts, J. Biol. Chem. **135**: 377, 1940.

The 17 patients studied can be divided into six different categories: 1. There were nine female pseudohermaphrodites, and in four of these the sex was in question at birth. These patients were all examined and the true sex determined by biopsy of ovaries. 2. One patient was a true hermaphrodite who showed signs of virilism at the age of 3 years. 3. Three genetic males whose disease had its onset before the age of 3 years were followed. 4. One male child had virilism with Addisonian-like symptoms, in whom the diagnosis was made at 15 months of age. 5. One adult with proved adrenal carcinoma had manifestations of both the adrenogenital and Cushing's syndrome, and one 11-year-old girl with virilism of one year's duration also had an adrenal carcinoma. 6. One girl demonstrated the syndrome of "precocious adrenarche."[6] This latter condition, of course, is not considered to be one of adrenal virilism.

Summary of Data in Fifteen Cases of the Virilizing Syndrome

Patient	Diagnosis *	Present Age	Hospital Treatment: Average Control 17-Ketosteroids	Hospital Treatment: Drug Dosage †	Hospital Treatment: Lowest 17-Ketosteroids	Hospital Treatment: Prolonged Administration †	Clinical Results
J. L.	Pseudo.	14	39.6	E., 100 mg. I. M., 4 days	9.6	E., 25 mg. I. M. daily, 17 mo.	Alleviation of severe acne; breast development
T. K.	Pseudo.	14	31.3	E., 200 mg. I. M., 4 days	11.2	E., 100 mg. I. M. twice weekly, 15 mo.	Minimal breast development; improvement in behavior
R. E.	Pseudo.	10	17.7	E., 100 mg. I. M., 5 days	3.8	E., 50 mg. P. O. daily, 8 mo.	Breast development; clitoris decreased to half control size
F. K.	Pseudo.	9	17.7	E., 75 mg. P. O., 7 days	6.9	E., 25 mg. P. O. daily, 8 mo.	Breast development; behavior improvement
C. B.	Pseudo.	17	28.8	E., 25 mg. I. M., 4 days	9.7	E., 25 mg. I. M. daily, 6 mo.	Menstruation
A. M.	Pseudo.	17	69.0	F., 200 mg. I. M., 7 days	3.8	E., 75 mg. I. M. three times weekly, 5 mo.	Menstruation
K. A.	Pseudo.	15	63.0	F., 100 mg. I. M., 6 days	6.0	E., 50 mg. P. O. daily, 14 mo.	Breast development; acne improved
B. L.	Pseudo.	2	9.0	E., 25 mg. I. M., 4 days	2.2	E., 12.5 mg. I. M. daily, 13 mo.	Slowing of accelerated growth rate
C. A.	Pseudo.; raised as ♂	16	63.0	E., 100 mg. P. O., 10 days	1.6	Not continued	.....
B. F.	True hermaphrodite	5	9.6	E., 50 mg. I. M., 4 days	2.7	E., 25 mg. P. O. daily, 11 mo.	Slowing of accelerated growth rate
A. R.	Macro.	9	19.2	E., 50 mg. P. O., 5 days	13.2	E., 37.5 mg. P. O. daily, 15 mo.	Behavior improvement
C. D.	Macro.	3	13.2	E., 50 mg. I. M., 4 days	4.7	E., 25 mg. P. O. daily, 13 mo.	Slowing of accelerated growth rate
W. H.	Macro.	4	19.7	E., 100 mg. P. O., 4 days	2.4	.....	.....
L. Y.	Macro.; Addisonian-like symptoms	3.6	12.4	E., 100 mg. I. M., 4 days	2.7	E., 10 mg. I. M. daily, 2 mo.	Clinically well; DCA ‡ therapy discontinued; accelerated growth slowed
A. B.	Precocious adrenarche	4½	5.0	E., 50 mg. I. M., 4 days	2.5	Not continued	.....

* Pseudo. = pseudohermaphrodite. Macro. = macrogenitosomia precox.
† E. = cortisone acetate. F. = compound F acetate. I. M. = intramuscularly. P. O. = by mouth.
‡ DCA = desoxycorticosterone acetate.

The underlying adrenal pathological condition in these patients was demonstrated to be bilateral adrenal hyperplasia either by biopsy or perirenal air insufflation. The 17-ketosteroid values were characteristically greatly elevated. It was further demonstrated that the administration of 75 to 100 mg. per day of corticotropin resulted in still further increases in the urinary neutral 17-ketosteroids. Since exogenous corticotropin can further stimulate these hyperplastic adrenals, one must assume that they are under endogenous corticotropin control.

RESULTS

1. *Female Pseudohermaphrodites.*—In all nine cases of female pseudohermaphroditism there was a prompt and dramatic decrease in the excretion of 17-ketosteroids as a result of the administration of cortisone or compound F (see the accompanying table). As little as 25 mg. per day of cortisone was sufficient to depress the steroids in an 18-month-old pseudohermaphrodite to almost normal levels. Higher doses, 50 to 200 mg., were administered to the older children, and they, too, proved effective. One patient (T. K.), aged 14, did not show a marked fall in urinary 17-ketosteroids while receiving parenterally 50 mg. of cortisone per day for four days. However, she did demonstrate some improvement in behavior with prolonged oral cortisone therapy (50 mg. per day), in that she became less surly and more cooperative. She also showed some evidence of breast development. She was subsequently readmitted to the hospital, where it was found that the parenteral administration of 200 mg. a day of cortisone suppressed the 17-ketosteroid excretion to values as low as 11.2 mg.

Prolonged oral cortisone acetate therapy was not effective as the parenterally administered suspension of cortisone acetate. J. L.'s 17-ketosteroids fell to 9.6 on 100 mg. per day of cortisone suspension. She was discharged on a regimen of 25 mg. per day (12.5 mg. twice daily) orally. Her 17-ketosteroids gradually rose to 48 mg. per day. The same dosage was administered in one daily injection, and her ketosteroid excretion again fell to 17 mg. within two weeks.

6. Wilkins,[5b] p. 144.

The most striking fall in 17-ketosteroid excretion, from 63 mg. per day to 1.6 mg. per day, occurred in patient C. A., a female pseudohermaphrodite who was raised as a boy after the surgical removal of the ovaries, tubes, and uterus, 10 years previously. At the present time there is a "penis" 8 cm. long; the patient is extremely hirsute and masculine in appearance. It is of interest that this marked decline to subnormal levels in the urinary 17-ketosteroids should occur in the one patient without gonads.

Some of the patients discussed above have been followed for sufficient length of time so that definite clinical changes have been noted. In the younger children, there was a slowing of the accelerated growth rates that were present before the onset of cortisone therapy. In the older girls, definite breast tissue made its appearance. Acne became markedly diminished in those patients exhibiting this condition before therapy. The alteration in 17-ketosteroid excretions and comments on the clinical responses are briefly summarized in the accompanying table.

2. *True Hermaphrodite.*—B. F. was thought to be a boy at birth because of an enlarged clitoris and lack of a vaginal orifice. More careful study at the age of 18 months, which included an exploratory operation and gonadal biopsy, revealed the presence of ovotestes, tubes, uterus, and vaginal canal, which ended in a urogenital sinus. At that time there was no evidence of virilism, and her 17-ketosteroid excretion was 3.0 mg. per day. However, one year later she commenced to grow at an accelerated rate and showed advanced maturation of her skeletal system by x-ray and pubic hair developed. Her 17-ketosteroid excretion rose to 10 mg. per day. Perirenal air insufflation did not reveal the presence of a tumor. Her ketosteroid excretion fell to 2.7 mg. per day during parenteral administration of 50 mg. of cortisone.

3. *Macrogenitosomia Precox with Addisonian-like Symptoms.*—This syndrome was first described by Wilkins, Fleischman, and Howard and by Thelander [7]; it is characterized by the presence of adrenal hyperplasia and a concomitant deficiency in retention of salt and water.

A male child, L. Y., was first seen at the age of 11 weeks because of persistent vomiting, diarrhea, and pronounced dehydration. He had not as yet regained his birth weight. His serum sodium was 119 mEq. per liter. Infusions of sodium chloride solution did not correct his hyponatremia until they were supplemented with desoxycorticosterone acetate (DCA). During treatment with 5 gm. of added salt and 5 mg. of desoxycorticosterone acetate intramuscularly, he showed remarkable clinical improvement and proceeded to gain weight and develop normally. A diagnosis of Addison's disease was made. At 15 months of age it was noted that his penis was enlarged, that he had a palpable prostate gland, and that his skeletal system showed an accelerated development. At that time urinary 17-ketosteroid values averaged 10 mg. per day, or about 10 times the normal value for a child of this age. It was at this time that the diagnosis of adrenal virilism with Addisonian-like symptoms was made. Subsequent perirenal air insufflation studies revealed bilateral enlargement of the adrenal glands. This patient continued to do well clinically while receiving 5 mg. per day of desoxycorticosterone acetate and added salt except for several bouts of acute tonsillitis, when he again showed signs of an "Addisonian crisis" with low serum sodium levels.

He was given a constant salt intake plus 5 mg. per day of desoxycorticosterone acetate and then cortisone. The metabolic effects of this therapy have been described.[4d] While he was receiving cortisone, it was possible gradually to decrease his requirement of desoxycorticosterone acetate and finally discontinue its use completely. At the time of reporting he was being maintained in good condition with 10 mg. of cortisone per day and approximately 5 gm. of added sodium chloride. Repeated analysis of the urinary 17-ketosteroids have revealed values of between 2 and 4 mg. per day. This patient has demonstrated the most remarkable clinical response to cortisone therapy of all in the series. He has grown normally, but there has been no decrease in the size of his genitalia.

4. *Macrogenitosomia Precox.*—Three patients who are classical examples of virilism in boys have been treated. In these patients there was no evidence of adrenal tumor. In one (C. D.) the parenteral administration of 25 mg. of cortisone suspension twice daily caused an almost immediate fall in 17-ketosteroids. In another (W. H.) 100 mg. did the same. The third patient (A. R.) demonstrates the greater efficiency of the parenterally administered cortisone. His 17-ketosteroids fell from 19.2 to 13.2 mg. during treatment with 25 mg. of cortisone orally (12.5 mg. twice daily); this was increased to 37.5 mg. per day (12.5 mg. three times a day), but, in spite of this, his 17-ketosteroid rose to over 20 mg. per day. The regimen was changed to 25 mg. per day in one injection, and within four days his 17-ketosteroids fell to 12 mg.

5. *Adrenal Carcinoma.*—A 42-year-old woman (K. C.) with hypertension, buffalo-type obesity, hirsutism, acne, beginning baldness, enlargement of the clitoris, and amenorrhea was studied at St. Luke's Hospital. She had no impaired glucose tolerance or osteoporosis. Her admission 17-ketosteroid excretion was 37.8 mg. per day. After completion of her hospital treatment, her 17-ketosteroids were 24 mg. With the parenteral administration of 100 mg. per day of cortisone there was no significant fall in the ketosteroid excretion. At operation an adrenocortical carcinoma with metastases was found.

An 11-year-old girl (A. P.) with a one year history of generalized hirsutism, acne, enlarged clitoris, voice change, and hypertension was admitted to Babies Hospital. There was no evidence of osteoporosis, diabetes, or thinning of the skin. Her urinary 17-ketosteroid values varied between 35 and 40 mg. per day. She was given a four day course of 100 mg. of cortisone daily intramuscularly, which had no appreciable effect on the level of the 17-ketosteroids. An intravenous pyelogram was reported as indicating no displacement of the kidneys; however, a perirenal aerogram revealed a large tumor anterior to the kidney. This was confirmed on exploration, when a large infiltrative carcinoma was found. No excessive amounts of dehydroisoandrosterone were de-

7. (*a*) Wilkins, L.; Fleischman, W., and Howard, J. E.: Macrogenitosomia Precox Associated with Hyperplasia of the Androgenic Tissue of the Adrenal and Death from Corticoadrenal Insufficiency: Case Report, Endocrinology **26**: 385, 1940. (*b*) Thelander, H. E., and Cholffin, M.: Neonatal Cortical Insufficiency (Addison's Disease) Associated with the Adrenogenital Syndrome, J. Pediat. **18**: 779, 1941.

monstrable in the urine of either patient by the sulfuric acid test [2b] or by chromatography.[8]

6. *Precocious Adrenarche.*—In some children a considerable amount of pubic hair may develop as early as 2 to 3 years of age. This may be followed by the appearance of a small amount of axillary hair at an early age, with no other signs of virilism. These girls show breast development and menstruate at a normal age, and the boys mature normally as well. This condition has been called precocious adrenarche or premature pubarche.

Patient A. B. was first seen at the age of 4½ years because of early appearance of coarse pubic and axillary hair. She was followed for almost a year and demonstrated no increase in clitoral size, no increase in stature above normal, and no acceleration of bone age. During this study on two consecutive days the values of urinary 17-ketosteroids were 5.5 and 4.4 mg. Fifty milligrams a day of cortisone was administered parenterally for four days, and the 17-ketosteroids declined to a value of 2.5. This latter value would be considered the upper limit of normal for a girl of this age.

COMMENT

The administration of cortisone to patients with adrenal pathological changes may serve as a diagnostic test for adrenal tumor. Fourteen patients with adrenal hyperplasia showed a marked fall of the urinary 17-ketosteroids with adequate cortisone administration. The two patients with adrenal carcinoma demonstrated no such fall. Venning [9] described a patient with an adrenal tumor in whom no fall occurred after the injection of cortisone. Moloshok [10] reported a similar lack of decline in urinary steroids in a patient with a proved adrenal adenoma that was responsible for signs and symptoms of virilism.

It is postulated that the fall in urinary 17-ketosteroids as a result of cortisone administration in patients with adrenal hyperplasia is due to inhibition of pituitary corticotropin secretion. Since this decline in steroid excretion does not occur in the presence of adrenal neoplasms, it would appear that these tumors are independent of corticotropin control. This difference in response to cortisone may very well serve as a diagnostic test for the presence of an adrenal neoplasm as contrasted to bilateral hyperplasia.

The administration of cortisone to patients with adrenal hyperplasia appears to be of definite benefit. Since the physical manifestations of this condition proceed slowly, sufficient time has not elapsed so that any dramatic change might be noticed in the patients. Wilkins [4b] and Bartter and co-workers [4c] have recorded the onset of menstrual periods in two girls (16 to 18 years of age) with this syndrome, during treatment with cortisone. At the time of writing, two of the five female pseudohermaphrodites described herein had begun to menstruate after cortisone treatment alone. Some degree of feminization had occurred, in the form of breast development, in the three others. The excretion of 17-ketosteroids had fallen to approximately normal levels in all patients.

In order to attain a remission in patients with rheumatoid arthritis or other "diseases of collagen," large doses of cortisone are administered. A state of hyperadrenalism must be achieved, which results in many of the so-called toxic manifestations of cortisone. From the available evidence, the mechanism of action of this steroid in adrenal hyperplasia is through the suppression of endogenous corticotropin secretion, with resultant adrenal "atrophy." It is not, therefore, necessary to administer large doses of cortisone. The administered cortisone substitutes for the abnormal steroids usually secreted by the adrenals in this syndrome. Under these circumstances, more physiological amounts of cortisone may be administered in an attempt to suppress endogenous corticotropin secretion. In none of these patients were such conditions as hypertension, edema, and glycosuria encountered.

Another interesting feature of these observations has been the relative inefficiency of the oral route of administration. For example, A. R. showed but minimal fall in 17-ketosteroid excretion while receiving 37.5 mg. per day (12.5 mg. three times a day) of cortisone orally, but after five days of intramuscular administration of 25 mg. of cortisone (in one injection), the 17-ketosteroid values fell 50%. J. L. also demonstrated a 60% fall in ketosteroid excretion when parenteral administration of cortisone (25 mg. per day in one injection) was substituted for the orally administered steroid (12.5 mg. twice a day) at the same dose level. It should be noted that psychological changes were noted by the parents of these patients, although the urinary steroid values had not fallen. The difference between the oral and parenteral routes may be due to the rate of absorption. Cortisone given orally is absorbed very quickly and may have its effect in a short period of time but is also inactivated quickly,[11] so that its span of action is much shorter than cortisone suspension, parenterally administered, which may reside at the injection site for some time.

Talbot and co-workers,[2a] Mason and Kepler, and Allen and associates [2b] have stressed the importance of excessive amounts of the β-ketosteroid fraction (dehydroisoandrosterone) as diagnostic of adrenal neoplasms. In neither case reported above were excessive amounts of this steroid found either by the sulfuric acid test of Allen or by chromatography.[8] It is apparent that tumors vary in the secretion of dehydroisoandrosterone.

According to Wilkins and co-workers [7a] the precocious appearance of axillary and pubic hair in girls is probably of adrenal origin. Therefore, it would be reasonable to assume that the administration of cortisone would cause a diminution in ketosteroids in patients with this condition as well.

The response in the 17-ketosteroid values following the injection of cortisone or compound F is different from that which occurs in the normal. Chronic administration of these compounds results in minor fluctuations in these values.[12] In patients with decreased values the 17-ketosteroid levels may rise,[12] and in Addi-

8. Dingemanse, E.; Huis in't Veld, L. G., and de Laat, B. M.: Clinical Method for the Chromatographic-colorimetric Determination of Urinary 17-Ketosteroids, J. Clin. Endocrinol. **6**: 535, 1946.

9. Venning, E.: Discussion in Proceedings of the Second Clinical ACTH Conference, Philadelphia, The Blakiston Company, 1951, p. 81.

10. Moloshok, R.: Personal communication to the author.

11. Louchart, J., and Jailer, J. W.: Inactivation of 11-Dehydro-17-Hydroxycorticosterone by Tissue Slices, Proc. Soc. Exp. Biol. & Med. **79**: 393, 1952.

12. Sprague, R. G., and others: Observations on the Physiologic Effects of Cortisone and ACTH in Man, Arch. Int. Med. **85**: 199 (Feb.) 1950.

13. Jailer, J. W.: Unpublished data.

sonian patients there is often a marked rise in the ketosteroid excretion levels during prolonged cortisone administration.[13]

SUMMARY

Fourteen patients with virilism due to bilateral adrenal hyperplasia were given either cortisone or compound F for various periods of time. In all 14 patients there was a dramatic fall in the total neutral 17-ketosteroid values within four to five days, from the elevated levels characteristic of this disease to amounts approximately normal for the age and sex of the patients. Long-term administration of these steroids resulted in the appearance of some feminine traits in the genetic females. None of the side-effects of cortisone toxicity were noted.

In two patients with proved adrenal carcinoma, the administration of cortisone was without effect on the excretion of 17-ketosteroids. It is postulated that the decrease in the ketosteroid excretion as a result of cortisone administration in the former group is mediated through pituitary inhibition of corticotropin (ACTH) and secondary "adrenal atrophy." On the other hand, adrenal cortical neoplasms are independent of ptuitary corticotropin control, and therefore pituitary inhibition is without effect on the tumor.

PAIN IN THE ANORECTAL REGION

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Although patients do not shrink from examination of the anus and rectum so much as they did a few years ago, even yet many of them do not accept it as a matter of course. Those who, because of false modesty, hesitate to undergo this examination are likely to defer consultation until discomfort is unbearable. By then, of course, valuable time may have been lost. When the patient seeks advice, whether he seeks it early or late, he is entitled to immediate, careful attention. The causes of pain in the anorectal region are many, but fortunately diagnosis usually is made easily. Nevertheless, complete examination, including sigmoidoscopy, should be performed before a patient is operated on or dismissed, even though the cause of discomfort may appear to be of anal origin. Only by application of thorough methods can a grave mistake be avoided if a patient harbors a serious lesion that is not revealed by superficial examination.

Of importance equal to that of examination is the taking of a thorough history. This should reveal the character of the pain, as well as its situation, duration, manner of onset, and relationship to defecation. A diagnosis should never be made from the history alone, and, even when thorough examination has been performed, the examiner should be sure that the abnormal physical findings explain the patient's complaint. Otherwise, treatment may be instituted for some obvious anal or rectal abnormality that is not the cause of the patient's chief disability. This is particularly likely to occur when the patient cannot give a lucid description of his discomfort. It may be wise to correct the obvious abnormal condition in spite of the fact that it bears no relationship to the chief complaint, but the patient should not be led to believe that he will thus be relieved of his main symptoms. All proctologists have seen patients who have unsuccessfully undergone multiple surgical procedures for pain in the region of the rectal outlet. In some cases, it appears that careful preliminary questioning would have obviated the treatment, which evidently could offer the patient little or no chance of relief. Worse yet, the discomfort may have increased during the period of repeated disappointments.

In some instances pain in the anorectal region may be extremely difficult to evaluate, and sometimes it may be wise to question and examine a patient on repeated occasions before reaching a decision as to the cause. When dealing with such difficult cases, frequently it is wise to seek the opinions of other physicians, such as urologists, orthopedists, gynecologists, neurologists, or psychiatrists. Also, examination performed while the patient is under anesthesia is indicated if the anus is extremely tender, spastic, or contracted. The same is true if it is suspected that an abscess is hidden and may be missed unless the musculature of the anus and lower portion of the rectum is relaxed more than it can be while the anus is sensitive to pain.

An important factor entering into the evaluation of any patient's complaint is his threshold of pain. There seems little doubt that a painful lesion does not produce an identical response in all persons. Furthermore, some patients minimize their complaints, while others magnify them.

After these general statements, it is appropriate to state that I do not propose to discuss pain as it is related to the neuroanatomy of the anorectal region. It should be noted, however, that the nerve supply of the rectum is derived from the visceral or autonomic portion of the nervous system and is not subject to ordinary pain stimuli. The anus and perianal region, on the other hand, derive their innervation from the somatic or cerebrospinal portion of the nervous system and are very sensitive to pain stimuli. It should be kept in mind that a given condition may cause different types of pain in different persons and that any one patient may suffer from multiple, coexisting conditions.

PERIANAL AND ANAL PAIN

Pain caused by lesions occurring in the perianal zone, but independent of the anus, usually is not appreciably affected by passage of feces, and, although in some instances it may be severe, it usually is described as "soreness," "smarting," or "a burning sensation." It may be experienced intermittently, sometimes only when pressure is applied to the region, or it may be

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present constantly. The patient usually is able to designate the site of discomfort with his finger. The terms the patient uses to describe pain of perianal origin may also be used by him to describe pain that originates in the anus. In contrast to the former type of pain, however, anal pain is definitely associated with defecation. Anal lesions, moreover, and conditions that cause protrusion of tissue through the anus, whatever the origin of the tissue, usually are accompanied by spasm of the sphincters. The spasm may initiate or increase the pain.

Soreness and Burning Discomfort.—The terms soreness and burning are used more or less interchangeably, by both physicians and patients. In general, however, the following differentiation can be made. Soreness may be the result of numerous conditions, among which are abrasions of the skin, inflamed condylomas, actinodermatitis, drainage from a sinus, contusions, and improper anal hygiene. Burning pain in the anal and perianal regions, either or both, may accompany several states, but it occurs oftenest as a result of some disease of the skin; this may vary from mild inflammation, such as commonly is associated with attacks of diarrhea, to severe dermatitis, such as may result from the trauma of scratching. Sensitivity to local medication may cause severe and sometimes widespread dermatitis, with accompanying excessive distress. Frequent offenders are the so-called analgesic ointments. In recent years, also, patients have been encountered who, after oral administration of certain antibiotics, complained of burning accompanied by itching. These symptoms may occur even in absence of the looseness and frequency of stools that the antibiotics may produce, and often there is no abnormality on inspection of the area other than mild cutaneous irritation. Any one period during which the patient is troubled by these manifestations usually is short, but the condition may recur periodically. As a cause of burning discomfort in the anal or perianal regions cryptitis has been overrated. This seldom occurs in the absence of other local pathological change.

Other conditions that may involve this region, and that must be remembered in connection with burning discomfort, are gonorrheal infections and the primary and secondary lesions of syphilis. Also, certain diseases of the nervous system, such as multiple sclerosis and tumors that cause irritation in the lateral tracts of the spinal cord, must be considered in the differential diagnosis. Pain in the anorectal region caused by these diseases is rare, but for this reason especially they must be kept in mind. It must not be forgotten either that pain, particularly of the burning type, which is frequently located in the perineum, need not be explainable on an organic basis. This is especially true of persons with perverted sexual habits.

Pain of Hemorrhoids and Polypoid Lesions.—The patient ordinarily does not complain of uncomplicated external hemorrhoids. The distress caused by thrombosed external hemorrhoids depends on the magnitude of the thrombosis, the amount of pressure exerted on the overlying skin, and on whether the hemorrhoid is so situated that the sphincter can contract on it. Uncomplicated internal hemorrhoids, hypertrophied anal papillae, and polypoid lesions that protrude through the anus only at the time of passage of feces cause little discomfort. However, when they remain prolapsed and become complicated by edema, thrombosis, erosion or gangrene and are accompanied by spasm of the sphincter, they may cause constant, severe throbbing or aching pain, which, as has been indicated, is accentuated by defecation.

Pain of Abscess.—The pain occasioned by abscess in the anal or perianal regions varies markedly, and its severity depends primarily on the size of the abscess, the amount of pressure on the overlying skin, and the proximity of the abscess to the sphincter muscles. The pain is usually constant, throbbing or aching in character, and may not be greatly affected by evacuation. Ischioanal abscesses, pilonidal abscesses that point in the perianal region, and ordinary furuncles, if large, usually are accompanied by intense pain. Small abscesses due to infected comedones and infected sebaceous cysts, on the other hand, frequently are attended by only mild to moderate soreness. Abscesses associated with hidradenitis suppurativa and those of the ischioanal variety that drain partially back through an anal crypt usually cause only moderate discomfort. This is owing to the small size of the abscesses and the consequent lack of pressure on the overlying integument.

Lancinating or Cutting Pain.—One condition that could frequently be diagnosed by history alone is anal fissure. The pain is characteristically intermittent and lancinating. It either starts or increases in severity in the course of defecation and continues afterward for a period varying from a few minutes to several hours. Sometimes the patient may state that the pain is constant but that it is greatly increased during and after bowel movements. However, the diagnosis of anal fissure should never be made from the history alone, for other less common conditions, such as epithelioma, anorectal adenocarcinoma, chronic ulcerative colitis, and regional enteritis can cause anal ulceration and produce the same type of pain. Abrasions and tears of the anal skin, which occur most commonly near the anal verge, and particularly in situations in which the anus is contracted, may cause sharp, cutting pain. This pain, however, is not so severe or lasting as that of anal fissure, and it tends to disappear after a few days, when the lesion has healed.

RECTAL PAIN

Often the patient's description of what he calls "rectal" pain is so indefinite that the proctologist has difficulty determining its nature or its location. Sometimes, as has been said, he must call on other specialists for assistance. Commonly, patients are unable to either describe or locate their rectal discomfort with any degree of accuracy. Also most lesions in and about the rectum do not cause pain unless they involve the anus or are sufficiently extensive to cause pressure or to produce spasm of the anorectal musculature. Consequently, a carcinoma of the rectum is often too far advanced for successful treatment by the time the patient seeks his physician's advice. On the contrary, some patients are cancer conscious, and it may be difficult to convince them that a malignant tumor is not present. Reassurance in such cases is much easier, of course, if a definite cause of the discomfort can be found.

I shall discuss rectal pain under two broad headings: (1) pain with definite characteristics, usually severe, and considered to be the immediate result of spasm of the intrinsic musculature of the rectum and (2) heterogenous pain that is vague and of which the cause is obscure.

Pain Caused by Spasm of the Rectal Musculature.—Tenesmus is a painful, ineffectual effort to evacuate the terminal portion of the colon. It may vary from a mild to an intense and constant desire to evacuate the rectum; it is attributable to spasm of the circular muscle of the rectum. Usually, the cause of the spasm is readily demonstrable as inflammation of the rectal mucosa, such as simple proctitis or proctitis associated with chronic ulcerative colitis, amebiasis, bacillary dysentery, or tuberculosis. Benign or malignant rectal neoplasms, particularly if extensive, impacted feces, and foreign bodies in the rectum also are likely to cause tenesmus. Occasionally rectal spasm is associated with diverticulitis or with benign rectal stricture if the mucosa is sufficiently inflamed; also, spasm accompanies extrinsic malignant conditions that extensively invade the rectal wall. Sometimes no cause for this complaint is demonstrable.

Proctalgia fugax is a term coined by Thaysen [1] for a condition characterized by paroxysms of sudden, agonizing pain in the region of the rectum. The pain usually lasts from 1 to 15 minutes; often it is accompanied by severe prostration. It occurs more frequently at night than in the daytime. A patient may experience such pain only once, but generally he gives a history of several attacks at intervals varying from days to years. It affects males who are 30 or more years of age more than others and seemingly is likely to afflict those who hold responsible positions. It is generally agreed that the immediate cause of the pain is muscular spasm, but opinion differs as to whether the spasm is in the region of the rectosigmoid, the rectum, or the internal sphincter. The site of the spasm probably varies from person to person, for there is difference of opinion among patients as to its exact situation. One may say it is about 1 in. (2.54 cm.) internal to the rectal outlet, while another may state that the distance from the outlet is 3 to 4 in. (7.62 to 10.16 cm.). The opportunity to examine patients in the course of an attack is rarely afforded. I doubt, however, that such opportunity would provide conclusive information concerning the site or the cause of the spasm. In some instances there may be a physical basis for the spasm, such as some abnormality of the prostate gland or seminal vesicles, but, in my experience, the condition is most frequently encountered in the presence of tension states. Irrespective of what may serve as the trigger mechanism, the condition occurs fairly commonly. Treatment of concomitant minor diseases of the anus or rectum usually does not relieve the attacks and may even aggravate them. Frequently, reassurance that no serious disease is present, in addition to the use of such measures as administration of antispasmodics and of hot retention enemas, will cause the attacks gradually to vanish.

Other diseases that may produce severe spasmodic rectal pain are tabes dorsalis and spinal cord tumors. In these conditions, the pain usually lasts longer than it does in proctalgia fugax and there are associated neurological findings. The complement fixation test may aid in the diagnosis of tabetic crises.

Vague Rectal Pain.—Vague rectal pain includes sensations of burning, pressure, or aching discomfort that the patient describes as being high in the rectum, within the pelvis, or even in the lower portion of the abdomen. It also includes pain that he says is rectal but that is situated in the region of the coccyx or buttocks. Frequently he is not certain where the discomfort is. The chief concern of the proctologist is, of course, to rule out rectal, or anal, abnormality as the causative factor, but he must also always be on the alert for extrarectal disease that could produce the symptom. In this connection, the value of thorough digital examination cannot be overemphasized. Tumors that lie anterior to the sacrum, perirectal abscesses, diseases that cause change in the consistency or contour of the prostate gland or seminal vesicles, abnormally placed endometrial tissue such as is characteristic of endometriosis, and inflammatory or malignant processes in the pelvis can cause pain in the rectal region. Their presence frequently would not be suspected were they not palpated through the rectum. There is usually nothing characteristic about the type of the discomfort caused by any of these conditions. In the case of endometriosis, however, there usually is a specific relationship to menstruation.

Thiele [2] has described another cause of obscure pain in the rectal region, particularly of women. The condition is now known as the "Thiele syndrome." In brief, this condition is characterized by tenderness and pain localized in the region of the lower portion of the sacrum and coccyx, or in the contiguous soft tissues and muscles. These symptoms are the result of tonic spasm of the levator ani and coccygeus muscles. Sometimes, in the hip and leg there is concomitant pain that is attributed to spasm of the piriformis muscle. The pain is not accentuated by defecation, but usually it is definitely associated with prolonged sitting or riding. Thiele emphasized the importance of searching for foci of infection in the anus and in the posterior urethra, prostate gland, and seminal vesicles of males, as well as in the urethra, bladder, and vagina of females.

Other causes of rectal discomfort, usually vague and described as a sensation of pressure, are incomplete evacuation, excessive enemas, concealed prolapse, injection treatment for hemorrhoids, postoperative scars, and application of radium. Finally, it seems probable that some obscure rectal pain must still be explained on the basis of neurosis.

SUMMARY

The cause of pain in the anorectal region usually is discovered readily, but diagnosis may be difficult. If either taking of the history or thorough examination is neglected, the patient may be denied necessary treatment or subjected to unwarranted treatment.

Anal or perianal pain may be described as soreness, smarting, burning, aching, lancinating, or cutting. It

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may be constant or intermittent and may or may not be increased by pressure or by defecation. Usually the cause is local, but it may be systemic; for this reason the examiner must search for the lesion both within and without the anus and rectum. Occasionally, an organic cause cannot be found.

Rectal pain may be attributable to muscular spasm, and this may be manifested by tenesmus or proctalgia fugax. Tabes dorsalis and tumors of the spinal cord may cause muscular spasm. Vague rectal pain may be described as burning, aching, or pressure pain and is likely to be indefinitely described as lying high in the rectum, low in the abdomen, in the pelvis, in the coccygeal region or in the buttocks. Among identifiable causes of such pain are anal disease, rectal disease, extrarectal disease, the Thiele syndrome, incomplete evacuation, excessive enemas, injection treatment, postoperative scars, and application of radium.

CLINICAL NOTES

LEPROSY

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and
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The word leprosy has cast a shadow of terror before it since times of antiquity. From biblical days, when the leper had to proclaim his presence with a cry of "unclean," to the present period, when he is summarily incarcerated, no other disease has had the tremendous religious, moral, and social implications of leprosy. Despite the fact that it is far less contagious than tuberculosis and infinitely less prevalent, leprosy is considered a much greater hazard by the general public and, perhaps, by the medical profession. If this attitude is found in the United States, with only 0.1% of the world's lepers, it is not difficult to conceive of the unfortunate lot of the remaining 5,000,000 lepers in the poverty-stricken, less enlightened areas of the world.

Recently, with newer advances in chemotherapy, a belated hope has been tendered to lepers. In view of the greater efficacy of these drugs in the initial stages of the disease, it is felt that emphasis on early recognition should be made to physicians who see this disease infrequently. For this reason, the following case report and a review of the salient features of leprosy are presented.

REPORT OF A CASE

A 54-year-old white man of Mexican descent was first seen at Alvin, Texas, complaining of fever and cough of three days' duration. Additional questioning revealed that the patient had been born in south central Texas and had lived in the Houston-Galveston area for the past 20 years, working as a laborer. Three years ago, several raised, pruritic lesions were noted over his forehead. Gradually, skin lesions spread over the patient's entire body. Slight difficulty in mastication and deglutition was noted with the slow but persistent development of lesions in the patient's mouth and throat. Six months before admission, the patient noted moderate weakness, occasional fever, and a weight loss of 20 lb. (9.1 kg.). When an acute respiratory infection developed, he came to the clinic. The past history was entirely noncontributory.

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Physical Examination

Physical examination revealed a well-developed, middle-aged man who showed evidence of weight loss and appeared chronically ill. The skin was characterized by innumerable brown, raised lesions varying from several millimeters to centimeters in size; the lesions were especially prevalent on the face, chest, back, and buttocks. The appearance of the head was striking (fig. 1), with large, pendulous, knobby ears, coarse, furrowed nodules on the brow, multiple brown nodular lesions over the face, and several pedunculate, soft, nonvascular nevi. In the pharynx, there was a diffusely nodular infiltration throughout the entire hard and soft palate (fig. 2), involving the uvula, which was enlarged and deviated to the left. Moderate, generalized lymphadenopathy

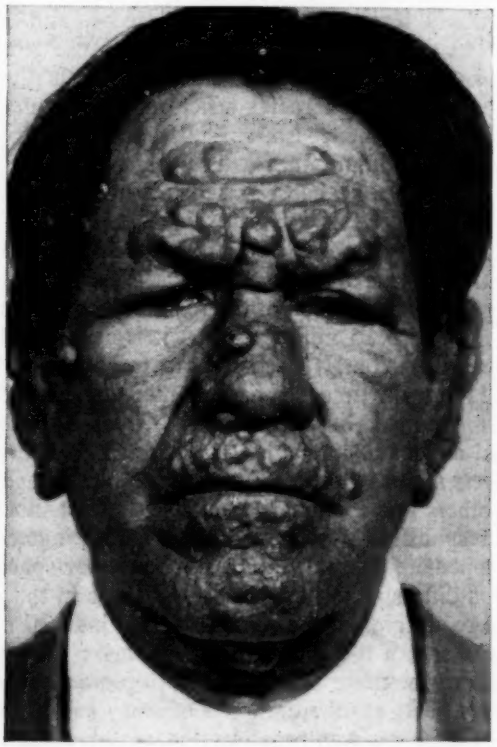

Fig. 1.—Multiple nodular lesions of the face and ears with leontiasis.

was present. The liver was palpable 2 cm. below the costal margin. Repeated neurological examinations showed normal results.

Laboratory Data

The positive laboratory findings included a hemoglobin level of 8.4 gm. per 100 cc. (photoelectric method) and an erythrocyte count of 3,370,000 cells. The sedimentation rate (Westergren method) was 34 mm. per hour. The albumin was 3.5 gm. per 100 ml. and the globulin 3.8 gm. per 100 ml. Scrapings from the skin lesions prepared with Ziehl-Neelsen's stain revealed acid-fast rods. Cultures of the organisms in Dubos' media produced no growth. Positive smears were easily obtained from nasal and pharyngeal scrapings. A biopsy of a nodule on the abdomen was reported as revealing a typical microscopic picture of Hansen's disease, lepromatous type. A sympathetic disclosure of the situation was made to the patient, and he was transferred to Carville, La.

COMMENT

Leprosy is a chronic, indolent, infectious disease of man caused by the Mycobacterium leprae. In contrast to the reaction to tubercle bacilli, the guinea pig is not sus-

ceptible to lepra bacilli, and no growth can be obtained on bacteriological media. In the United States, leprosy is found primarily in California, Texas, Florida, and Louisiana. The incubation period varies from 1 to 10 years, and the disease is most generally found in persons in their thirties.[1] Distribution within the body is by routes of hematogenous, lymphatic, and direct dissemination.

The newer South American classification includes the tuberculoid, lepromatous, and nonspecific types. The tuberculoid lesions are the neural leprids, comprising maculoanesthetic lesions with nonspecific inflammatory changes, plasma cells, fibroblasts, and lymphocytes. The lepromatous forms show chronic granulomatous lesions of the skin containing numerous bacilli as well as visceral involvement. The nonspecific type is considered a transitional form.

The clinical course in leprosy varies considerably. Lepromatous forms are usually initiated with vague prodromata of weakness, weight loss, malaise, and myalgia. Macular and nodular lesions appear on the forehead, ears, cheeks, and limbs. Early involvement is seen in the mucous membranes of the nose, pharynx, and larynx, with subsequent nasal discharge, dysphagia, and cough. The progression of nodules and folds on the head produces the characteristic leontiasis, accentuated by loss of the eyebrows. Visceral involvement is frequent, with granulomatous infiltrations into the liver, spleen, bone marrow, and adrenals. In the neural form, the earliest lesions are generally erythematous or hypopigmented maculae, the leprids. The central area is atrophic, depigmented, and anesthetic to touch, pinprick, and heat. With progression and involvement of peripheral nerve trunks, degenerative changes occur, and segmental loss of sensation prevails.

The diagnosis of leprosy is relatively simple, providing it is considered. Scrapings from the edge of a nodule in the lepromatous form reveal numerous acid-fast bacilli, with pathological confirmation by biopsy. Smears from involved mucous membranes are positive in almost all cases. Neural or tuberculoid disease frequently does not reveal bacilli. Diagnosis must be made on the findings of the circinate leprids with the central anesthetic area, evidence of peripheral involvement, and neurotropic disturbances. The differential diagnosis must include ringworm, syphilis, lupus vulgaris, tuberculosis, rhinitis, malaria, sarcoid of Boeck, vitiligo, neurofibromatosis, and syringomyelia.

For many years, the treatment of leprosy was based on various uses of chaulmoogra oil.[2] The discovery of newer agents, however, has radically changed the course and future of therapy in leprosy. Prominent among them are the sulfones, derivatives of the parent radical, 4,4′ diaminodiphenylsulfone; these drugs include glucosulfone (promin®) sodium, sulfoxone (diasone®) sodium, thiazolsulfone (promizole®), and sulfetrone (4,4′-bis [gammaphenyl-N-propylaminodiphenylsulfone tetrasodium sulfonate]).[3] The earlier effects of the sulfones include healing of the mucous membranes, improvement of eye conditions, and an increased sense of well being.[4] Later results include the subsidence of nodules and inflammatory lesions and the regrowth of hair. Streptomycin [5] has found its most important role in topical use in wet dressings. The other antibiotics, including aureomycin,[6] have all been valuable in controlling secondary infections and lessening the extent of required surgery. More recently, encouraging reports have been made of the effects of promacetin® [7] (sodium 4,4′-diaminodiphenylsulfone-2-acetylsulfonamide) and the thiosemicarbazones.[8]

Although all forms of therapy require months or years, the increasing interest in leprosy and the encouraging number of therapeutic agents available open an entirely new vista to the leper. With it must come a more enlightened attitude toward this disease by both the medical profession and the laity. As recently as 1948, handling of lepers was included in "hazard pay" with glider, parachute, and submarine rescue and demolition of explosives by the military service. In the same year, several unique events occurred at the National Leprosarium in Carville, La. For the first time, a patient received a medical discharge while in the communicable stage of the disease; the patient was followed by a private physician, who gave monthly reports. Also, symbolically, the barbed wire was removed from the fence around the hospital. In addition, a patient was discharged after 6 negative bacteriological examinations instead of the previous 12.[3]

Fig. 2.—Nodular infiltrations of the palate and uvula with displacement to the left.

These measures represent a gradual breach in the wall of ignorance, stigma, and therapeutic nihilism that has surrounded the victims of leprosy. The responsible authorities should see that adequate educational measures are instituted for the laity and the medical profession to acquaint them with the facts. Leprosy is less hazardous to both the patient and those exposed to him than some more common diseases. Newer forms of therapy offer hope to lepers, particularly in the early stages of the disease. Physicians must recognize leprosy in its primary form, and the leper must be taught not to conceal his affliction and to avoid confinement. Instead, he must learn that a sound medical program will be offered to him with an excellent chance of restoration to society

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in minimum time. Perhaps, as an additional adjunct, an exception could be made to the usual anathema to medical eponyms with the substitution of "hansenosis" or Hansen's disease for leprosy. The latter word will be slow to gain an aura of respectability after centuries of connoting stigma, social prejudice, and hopelessness.

SUMMARY

A case of lepromatous leprosy is reported with a review of the salient features of the disease. The marked improvement in the prognosis of leprosy with the newer forms of chemotherapy is emphasized. A plea is made for earlier recognition of the disease, with a more enlightened attitude by both the laity and the medical profession.

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CHRONIC ARSENIC POISONING FOLLOWING USE OF AN ASTHMA REMEDY

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Arsenic poisoning has been known since ancient times. Popular during the Middle Ages as a homicidal agent, arsenic is now a rather frequent cause of poisoning following the accidental ingestion of matches, insecticides, or rat poisons.[1] Inorganic arsenic is still used in treatment of a variety of diseases. It is recommended for the therapy of lichen planus [2] and psoriasis.[3] It is often effective as a palliative in treatment of chronic myelogenous leukemia, because of its activity in depressing the formation of leukocytes.[4] Recently, two patients with severe cutaneous manifestations of chronic arsenic intoxication were reported.[5] Both had been treated for bronchial asthma with remedies containing Fowler's solution. The following case history illustrates arsenic intoxication of a severer degree, apparently resulting from chronic ingestion of a similar mixture containing Fowler's solution.

REPORT OF A CASE

Mrs. G. M., a 41-year-old white woman, was referred to the Cedars of Lebanon Clinic, with the diagnosis of arsenical hepatitis, on March 17, 1950. She had been in good health until the onset of bronchial asthma five and one-half years earlier. From its onset the asthma was resistant to treatment, and the patient had episodes of sustained bronchospasm lasting several weeks and no periods of complete relief. In July, 1947, two years and nine months prior to admission, she consulted a clinic in Mississippi. After three days on the regimen prescribed by this clinic she obtained great relief, claiming to be "completely free of asthma for the first time." After a few days she returned home, taking with her the liquid "asthma mixture" dispensed by the clinic. She ingested 4 teaspoons of this medicine daily for the next 9 months. She then reduced the dosage to 2 teaspoons daily, occasionally doubling the dosage for a few days when wheezing recurred. She continued to take this medicament for a total of two years and four months, until November, 1949, refills being obtained by mail from the clinic at the patient's request.

In August, 1948, 13 months after starting to use the "asthma mixture" the patient noticed increasing freckling of the skin and darkening of the nipples. She experienced intermittent bouts of nausea, cramps, and diarrhea, which became progressively severer and more frequent. Early in 1949, symmetrical, tender hepatomegaly was noted. In succeeding months patches of thickened skin developed on her palms and soles, and she noted redness and puffiness about her eyes. In November, 1949, arsenic intoxication was suspected by her physician. Studies revealed the arsenic concentration in the patient's hair to be 2,900 μg. per 100 gm., as compared with the normal of only 60 μg. per 100 gm.[6] A skin biopsy showed melanosis. Gastrointestinal roentgenograms were normal. Ingestion of the "asthma mixture" was stopped at this time, because it was discovered that it contained Fowler's solution. The patient began using it again after five weeks, however, when her severe asthma that did not respond to other treatment. In January, 1950, she noted paresthesias and slight weakness of both hands and was again persuaded not to use the "asthma mixture."

Examination of the patient on admission to the hospital revealed heavy freckling of the skin, especially over the trunk and neck. The nipples and areolas were deeply pigmented. On the soles and palms there were several discrete hyperkeratotic patches. Conjunctival injection and periorbital edema were present. There was an increase in the posteroanterior chest diameter, and generalized sibilant and sonorous expiratory rales were heard. The heart was normal. The blood pressure was 100 mm. Hg systolic and 70 mm. Hg diastolic. The liver extended 5 cm. below the right costal margin and was extremely painful when palpated. The spleen was not felt. There were no definite objective neurological abnormalities, but the patient continued to complain of paresthesias.

Results of urinalysis were normal. There was neither anemia nor leukopenia, but the differential white blood cell count showed 10% eosinophils. The serum albumin was 4.1 gm. per 100 cc. and serum globulin 2.2 gm. per 100 cc. The total cholesterol content was 212 mg. per 100 cc., with the esters constituting 70%. The prothrombin time was 92% of the control. Cephalin flocculation was 1+ in 24 hours and 2+ in 48 hours. Thymol turbidity was 6.3 units. The sulfobromophthalein (bromsulphalein®) sodium test revealed 12% retention of a 5 mg. dose in 1 hour. The urinary arsenic level was 1.08 mg. per liter during a course of dimercaprol (BAL) therapy and 0.52 mg. per liter after cessation of dimercaprol therapy (the normal is 0 to 0.15 mg. per liter). A biopsy of the liver showed minimal fatty changes; the liver cells appeared swollen, and there were many binucleated forms. In a few areas there were small foci containing no liver cells. There were rare focal collections of leukocytes. In the portal areas there was a small increase in fibrous tissue.

The patient received two courses of dimercaprol therapy and was placed on a high protein, high caloric diet. The liver gradually decreased in size, and the gastrointestinal complaints subsided. Over a period of months the pigmentation lightened, but the hyperkeratotic condition remained. The asthma, during the 15 month follow-up period, remained difficult to control.

COMMENT

The clinical impression of chronic arsenic intoxication with melanosis, keratosis, gastroenteritis, hepatitis, and mild neuritis is substantiated by the high urinary arsenic level occurring in response to dimercaprol therapy and the extremely high arsenic content of the hair as well as the history of prolonged ingestion. The "asthma mixture" used by the patient contained 8 cc. of Fowler's solution per 6 oz. (177.4 ml.), which is equivalent to 0.44 mg. of arsenic trioxide per cubic centimeter. It has been stated by the clinic that this medicine has been given in about 10,000 cases without serious results. The

From the Cedars of Lebanon Hospital.

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usual duration of treatment is about 2 years, although some patients have taken the medicament for as long as 5 or 10 years.

In the case reported, the patient was supplied with the arsenical mixture for almost three years without being reexamined. The statement from the clinic that prescribes and dispenses the medicament that there were no serious toxic effects in 10,000 patients seems unacceptable in view of the lack of follow-up investigation. It is hoped that this report will serve as a warning to physicians whose patients may be exposed to this or other "low concentration" sources of arsenic for prolonged periods.

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ORALLY ADMINISTERED CORTISONE IN ERYTHEMA NODOSUM

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Erythema nodosum is a disease characterized by transitory nodules on the skin that resemble bruises; there is often fever, with or without migratory arthritis. In the older literature, erythema nodosum was considered a common expression of tuberculosis and rheumatic fever [1]; in patients with erythema nodosum in whom definitive evidence of tuberculosis or rheumatic fever could not be demonstrated it was nevertheless common practice to regard these patients as suspect. At present, it is known that erythema nodosum occurs with numerous diseases, including tuberculosis, rheumatic fever, streptococcic infections, coccidioidomycosis, infectious exanthems, sarcoidosis, syphilis, gonorrhea, leprosy, lymphogranuloma venereum, chancroid, and drug sensitivities. It is regarded as a disease of hypersensitivity in which the sensitizing agent may be bacterial, toxic, or chemical.[2] The severity and duration of the disease vary. Usually, recovery occurs in two to five weeks after onset, but the illness may last for months.

With the change in concept of the etiology of the disease therapy with cortisone or corticotropin (ACTH) appears eminently logical, since these agents are used successfully in treating hypersensitivity reactions. Several reports of treatment with these hormones have been published,[3] but the number of cases reported is small, and there are comparatively few reports detailing results of the oral administration of cortisone. Ureles and Kalmansohn [3b] and Albright and Kuffel [3g] reported single cases of erythema nodosum that were effectively treated by orally administered cortisone; both patients responded to the hormone favorably after unsuccessful results with penicillin and other agents. In the following case of erythema nodosum cortisone administered orally constituted the sole therapy.

REPORT OF A CASE

A 10-year-old girl was brought to my office on May 3, 1952, because of painful red swellings on her legs and right forearm. From April 10, 1952, to April 13, 1952, she had been confined to bed at home with a sore throat and a low grade fever, for which the only medication administered was three acetylsalicylic acid ("aspirin") tablets, 15 grains (0.97 gm.). On April 13, she resumed full activity, without symptoms. On April 26, 13 days after subsidence of throat soreness, a painful red swelling appeared on the mid one-third of the left leg, on the anteromedial aspect. On the following day additional, similar swellings appeared in the same vicinity as well as in a comparable area of the right leg and on the posterior aspect of the right forearm. Walking became impossible on account of severe pain. Her temperature was 102 F. The swellings became more painful and discolored, and the febrile course continued. There was no history of chorea, rheumatic fever, or "growing pains," and she had had few sore throats. The family history was noncontributory.

Physical examination revealed an acutely ill, underweight girl. Her temperature was 101 F and her pulse rate 128 per minute. She was unable to stand or walk because of pain in the lower extremities, and her knees were held in flexion. The lower two-thirds of the left leg was moderately edematous, and there were several raised, erythematous nodules in this area, chiefly on the anteromedial surface. The nodules were extremely tender. Similar lesions were present on the anteromedial surface of the right leg but were fewer in number. These nodules varied in diameter from 2 to 8 cm. Smaller areas of involvement were found on the medial surface of the right knee and on the mid one-third of the ulnar aspect of the right forearm. The patient's tonsils were small, and her pharynx appeared normal. Her heart rhythm was regular, 128 per minute, and the sounds were of good quality; there were neither murmurs nor thrills. There was no evidence of joint involvement.

Fluoroscopic and x-ray examination of the chest revealed no cardiac or pulmonary abnormality; the hilar shadows were not exaggerated. The electrocardiogram was normal, and the PR interval was 0.16 seconds. The hemoglobin and the red cell count were within normal limits. The white cell count was 12,000 per cubic millimeter, with a normal differential pattern. The sedimentation rate was 15 mm. in one hour (Cutler). The blood Wassermann reaction was negative.

The patient was promptly placed on cortisone administered orally. On the first day of treatment (May 3, 1952), 75 mg. was administered in three doses of 25 mg. each, at six hour intervals. On the second and third days, 25 mg. was administered twice daily. Thereafter, 25 mg. daily was given on the fourth to seventh days inclusive. On the first day of cortisone therapy relief of pain was evident after the third dose, approximately 13 hours after the ingestion of the first tablet. After 48 hours of treatment all pain and tenderness of the lesions cleared; there were no longer any visible nodules; and the previous erythematous areas became light brown. The patient at that time became fully ambulatory. On May 9 (the seventh day of treatment) the extremities appeared normal except for the finely wrinkled appearance of the skin of the left leg. Cortisone therapy was then discontinued, after seven days of treatment, during which 275 mg. of cortisone had been administered. On May 16, 1952, 0.97 gm. of acetylsalicylic acid was administered in an attempt to rule it out as the offending agent in this case. Repeated observations failed to disclose any recurrence of erythema nodosum. Approximately two weeks after termination of cortisone therapy tuberculin tests were negative (first and second strength purified protein derivative).

SUMMARY

Orally administered cortisone proved effective in treating a patient with a severe case of erythema nodosum; improvement became evident less than 24 hours after inception of treatment. After discontinuance of treatment there was no recurrence of the lesions.

840 Grand Concourse.

1. Favour, C. B., and Sosman, M. C.: Erythema Nodosum, Arch. Int. Med. **80**: 435-453 (Oct.) 1947.

2. Farber, S., and Mandelbaum, H.: Use of Cortisone in Erythema Nodosum, Arch. Int. Med. **88**: 395-399 (Sept.) 1951.

3. (*a*) Alpert, L. K.: The Collagen Disorders, Mod. Med. **19**: 51-58 (July 1) 1951. (*b*) Kierland, R. R.; O'Leary, P. A.; Brunsting, L. A., and Didcoct, J. W.: Cortisone and Corticotropin (ACTH) in Dermatology, J. A. M. A. **148**: 23-26 (Jan. 5) 1952. (*c*) Downing, J. G.: The Use of ACTH and Cortisone in Dermatology, New England J. Med. **246**: 56-65 (Jan. 10) 1952. (*d*) Downing, J. G.: The Use of ACTH and Cortisone in Dermatology, ibid. **246**: 94-101 (Jan. 17) 1952. (*e*) Beerman, H.: Erythema Nodosum, Survey of Some Recent Literature, Am. J. M. Sc. **223**: 433-446 (April) 1952. (*f*) Ureles, A. L., and Kalmansohn, R. B.: Oral Administration of Cortisone in a Case of Erythema Nodosum, New England J. Med. **245**: 139-140 (July 26) 1951. (*g*) Albright, R. W., and Kuffel, M. J.: Erythema Nodosum: Treatment with Cortisone by Mouth, California Med. **75**: 368-369 (Nov.) 1951.

THALLIUM INTOXICATION

REPORT OF TWO CASES

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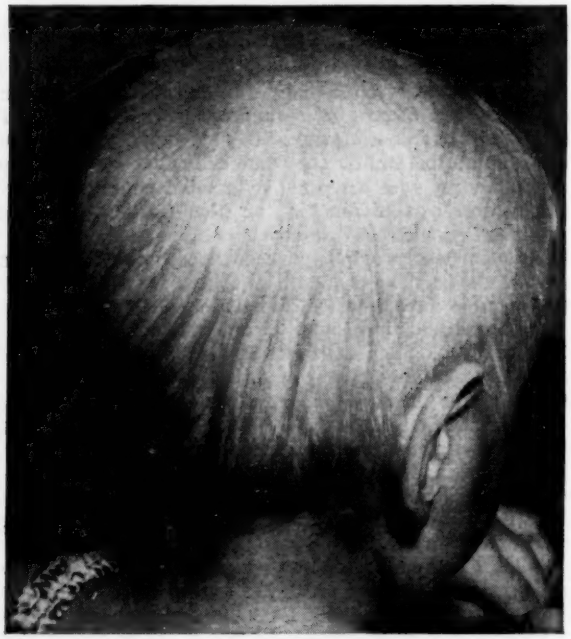
Rodenticides containing thallium salts are readily obtainable by the general public. The products are made in the shape of nuts or similar forms, in order to make them attractive to the rodents. When put up in such a manner, the agent is equally attractive to young children. Mazzei and Schaposnik,[1] Welty and Berrey,[2] and Grulee and Clark [3] have recently reported cases of thallium poisoning in children. We are reporting herein two additional cases of thallotoxicosis. The first signs of poisoning in these cases was alopecia of the scalp. These cases are reported to emphasize further the need for physicians to be on constant watch for this condition.



Alopecia in patient P. C. The photograph was taken on July 10, 1951, 26 days after the onset of alopecia.

REPORT OF CASES

N. C., a 3-year-old white girl, had been completely well until the evening of June 13, 1951, when her mother noticed a small area of baldness on the top of her head. By the following morning the bald area was about 5 cm. in diameter. The remaining hairs on the head could be pulled out with little tension and without discomfort to the child. At this time, P. C., the first patient's 2-year-old sister, was found to be losing her hair also. She, too, had been well until the onset of the present illness (see figure).

The results of neurological and physical examination of N. C. were completely negative except for the alopecia involving the scalp. The eyebrows, eyelashes, and hairs of the rest of the body were not affected. A hemogram revealed 9,450 white blood cells, 3,700,000 red blood cells, 11.3 gm. hemoglobin, and a color index of 0.96. The red blood cells and platelets appeared to be normal. The differential count revealed 28% polymorphonuclear leukocytes, 69% lymphocytes, and 3% monocytes.

Examination of P. C. revealed one other positive finding. There was moderate bilateral ptosis of both upper eyelids. The parents had noted the ptosis in the preceding 24 hours. The results of the rest of the neurological examination and general physical examination of P. C. were negative. The hemogram was as follows: white blood cells, 15,600; red blood cells, 3,700,000; hemoglobin, 11.8 gm., and color index, 1.0. Red blood cells and platelets appeared normal. The differential count showed 35% polymorphonuclear leukocytes, 59% lymphocytes, 5% monocytes, and 1% eosinophils.

Examinations revealed no fungi in either child and examination with Wood's lamp revealed no fluorescence. The parents were questioned about the possible ingestion of poisons. It was recalled that about two weeks preceding the illness an empty can of rodenticide had been found in the children's play area. The rodenticide had been used some time previously to kill moles. The can had contained a small number of peanuts coated with a blue substance. The children apparently had found the can and eaten the remaining contents. The manufacturer of the rodenticide revealed that the blue coating on the peanuts contained 1% thallium sulfate. The parents were unable to recall any evidence of illness at the time the empty can was found.

Urine was collected over a period of 24 hours from each child on June 15 (two days after the onset of alopecia) and examined for thallium. No traces of the substance were found.

The ensuing courses in the two patients were identical. In the following week they lost most of their scalp hair. No other hairy areas were involved. By the end of the second week after the onset of the alopecia, new hair growth was evident in the older child, N. C. The ptosis in P. C. was unchanged after one week; by the end of the second week it was gone. Definite regrowth of hair was first noted in P. C. 33 days after the onset of alopecia. No other abnormal findings were subsequently noted in either patient at any time, and the regrowth of hair appeared to be at a normal rate.

COMMENT

The diagnosis of thallotoxicosis in these two patients could not be substantiated by the observation of thallium in their urine. It would be expected, however, that thallium would not be recovered when the signs of poisoning appeared so late. Several factors point to thallium intoxication as the correct diagnosis: the history elicited from the parents, the lack of other signs and symptoms of diseases that could cause alopecia either primarily or secondarily, and the involvement of the peripheral nerves in one of the patients.

SUMMARY

Two cases of thallium intoxication, with resulting alopecia in both and nervous involvement in one, are reported. Both patients recovered completely.

1 Bryant Crescent (Dr. Hirsch).

1. Mazzei, E. S., and Schaposnik, F.: Subacute Poisoning by Thallium Treated with BAL, Brit. M. J. **2**: 791-792 (Oct. 8) 1949.

2. Welty, J. A., and Berrey, B. H: Acute Thallotoxicosis: Report of 2 Cases Treated with BAL, J. Pediat. **37**: 756-758 (Nov.) 1950.

3. Grulee, C. G., Jr., and Clark, E. H.: Thallotoxicosis in Preschool Nursery: Report of 4 Cases, A. M. A. Am J. Dis. Child. **81**: 47-51 (Jan.) 1951.

Eosinophil Response Tests.—Despite careful technique, individual eosinophil response tests are very inaccurate. . . . Greater than 50% drop of eosinophils has been noted following epinephrine or ephedrine in patients with pituitary tumors and in patients adrenalectomized and receiving small doses of cortisone. Responses of less than 50% are seen in a large number of patients with unrelated pathological conditions. Tests with these substances are therefore of little value in the diagnosis of adrenal, hypothalamic, or pituitary disease, and do not accurately assess the functional capacity of these organs at the time of examination.—W. R. Best, M.D., R. C. Muehrcke, M.D., and R. M. Kark, M.D., Studies on Adrenocortical Eosinopenia: A Clinic and Statistical Evaluation of Four-Hour Eosinophil Response Tests, *The Journal of Clinical Investigation*, July, 1952.

FOOTREST DEVICE FOR EXERCISING OF THE LOWER EXTREMITIES BY BEDRIDDEN PATIENTS

Joseph O. Smigel, M.D.
and
John H. Gibson, R.N., Pinewald, N. J.

We have constructed an apparatus that provides a means of exercising the feet and legs, can act as a footrest for comfort, and yet can be slid out of the way by the patient when not in use.

The construction is simple. It is inexpensive and can be made by anyone or in any home workshop. The model we use consists of: (1) a 12 in. length of 1½ in. hard rubber tubing padded with cellucotton® (absorbent cellulose composition resembling cotton) to three inches and covered by stockinet, and (2) a length of sash cord.

The sash cord is passed through the rubber tube and is of sufficient length to be tied to the springs on both sides of the bed, approximating the patient's hips, and leaving the padded footrest in a position that is comfortable for the patient. With the footrest in position, the patient is able to roll and push it on the bed approximately three to four inches. He can use the toes or heels to obtain support or to bring into play the various leg muscles. The length of travel will be determined by the thickness of the mattress; also, the mattress will give a certain amount of resistance to the exerciser.

Exerciser and footrest at rest position.

The footrest need not be made of hard rubber tubing as we used; any light metal tubing or a drilled wooden dowel can be substituted. The prime factor of the hole is that it be large enough to permit the footrest to slide freely. The padding can be of foam rubber, cotton, cloth, or any soft material, the amount depending on the size desired and the size of the tube. By providing hooks on the end of the rope, a change in the position of the rope may be made easier for the patient. By addition of a spring to both ends, added resistance would be obtained; by use of a rubber cord, greater flexibility and distance would be obtained.

We feel that this combination exerciser and footrest is very practical, cheap enough to be within the financial reach of anyone needing a lower extremity exerciser (the total cost runs between 50 cents and $1.00), and should prove an important means of providing much needed exercises for the bed patient.

Medical Director (Dr. Smigel) and Registered Physical Therapist (Mr. Gibson), Pinehaven Sanitarium.

SPECIAL ARTICLE

Cancer has now risen to second place among the causes of death in the United States. Studies hitherto sponsored by the Committee on Research of the Council on Pharmacy and Chemistry of the American Medical Association have dealt exclusively with the treatment of inoperable mammary cancer by means of steroid hormones and allied substances. This symposium of six papers on early diagnosis of cancer seeks to present a more hopeful realm of investigation.

Some biostatisticians have challenged presently accepted criteria for surgical intervention in certain forms of cancer on the ground that the end results over several decades have not altered the ultimate course nor added to the patient's term of life. This opinion is based on the fact that no significant decrease has occurred in the age specific incidence of these cancers in the mortality tables. Most oncologists feel that a time must exist early in the life cycle of a cancer when removal of the primary source would effect a cure. The office of the Committee on Research has requested this series of articles to offer to the medical profession a resumé of present day methods for the early diagnosis of cancer in the various organ systems. The final treatise in the group considers one of the most poignant problems of practice, the end care of the hopelessly ill cancer patient. The hope is expressed that by wider employment of the methods discussed and by further improvement in techniques, the inexorable course of cancer may be altered.

The articles will be published in successive issues of THE JOURNAL *until the series of six is complete.—Ed.*

SCREENING FOR CERVICAL CANCER IN INTERNIST'S OFFICE BY ROUTINE VAGINAL SMEARS

Maurice Fremont-Smith, M.D.
and
Ruth M. Graham, B.S., Boston

"Only the beginnings of cancer permit a cure," said Celsus in 25 A.D. In a consideration of carcinoma of the cervix, physicians must ask themselves whether present therapy is effective, whether women who are discovered to have this disease today can hope to live 10 years, whether a greater proportion of the 16,000 comparatively young women dying in this country every year of cervical cancer can be saved, whether the detection of carcinoma in situ is the key to greater salvage, and whether carcinoma in situ is an early manifestation of cancer or a reversible noncancerous lesion. At present earlier diagnosis is our only means of reducing the mortality from this disease. Jones [1] writes, "Stage I cancer of the cervix . . . can be cured in 80% of all patients and international Stage O cancer in approximately 100%; yet the general survival rate from carcinoma of the cervix is in the neighborhood of 30%, because of a preponderance of advanced cases." Table 1 records the stages at which the disease is diagnosed, as reported from clinics in this country and abroad. Even the most recent figures from American clinics show that in only one woman out of three is can-

The bibliographical references have been omitted from THE JOURNAL because of lack of space; however, they are included in the authors' reprints.

From the Vincent Memorial Laboratory of the Vincent Memorial Hospital, the Gynecologic Service of the Massachusetts General Hospital.

Dr. Herbert L. Lombard made available the New York State Age-Specific Incidence Ratio for Cancer of the Uterus, 1945-1947.

cer of the cervix diagnosed in stage 1. In two-thirds of the patients cancer is in an advanced stage when discovered. Recovery rates for stage 1 cervical cancer are given in table 2. In only one clinic did 80% survive, and this rate was based on relatively few cases. The majority of five year survival rates fall below 70%. Ten year survival rates average between 40 and 50% for stage 1 cervical cancer. Thus only one woman out of six discovered to have cervical cancer may expect to live 10 years of life. Only by earlier diagnosis can a higher survival rate be achieved.

TABLE 1.—*Distribution of Cases by Clinical Extent (International Classification)*

	Total No. of Cases	Percentage of Cases in Stage 1
League of Nations *		
1913-1943		
All countries	41,036	13
American clinics	9,012	16
1939-1943		
All countries	14,686	16
American clinics	2,658	22
Radium Centre, Copenhagen †		
1922-1939	4,027	13
Radium Institute, Edinburg ‡		
1940-1944	1,646	6
University of Minnesota §		
1939-1947	297	32
University of California ‖		
1948	555	20

* Annual Report on the Results of Radiotherapy in Carcinoma of the Uterine Cervix, Stockholm, 1951.

† Truelsen, F.: Cancer of the Uterine Cervix: Clinical Features with Particular Reference to the Results of Radiotherapy: A Report of 2,918 Cases, London, H. K. Lewis & Co., Ltd., 1950.

‡ Paterson, R.; Tod, M., and Russell, M.: The Results of Radium and X-Ray Therapy in Malignant Disease, Baltimore, Williams & Wilkins Company, 1950.

§ McKelvey, J. L.; Strenstrom, K. W., and Gillam, J. S.: Results of an Experimental Therapy of Carcinoma of the Cervix, Am. J. Obst. & Gynec. 58:896-907, 1949.

‖ Morton, D., in discussion on McKelvey, Strenstrom, and Gillam.§

One factor precluding early diagnosis is delay between onset of symptoms and the first visit to the physician. Maliphant [2] found advanced disease in 60% of women reporting six months after onset of symptoms. Only 10% came for treatment within three months of onset of symptoms, and advanced disease was already present in 50% of this group. Moreover, in many cases no symptoms appear until late in the disease. Truelsen,[3] on the basis of 4,000 cases, says: "Even under the most favorable circumstances, when the patient sees a doctor as soon as she has noticed her first symptoms, the doctor makes the correct diagnosis at once, and the patient is at once referred to treatment which is instituted immediately, more than 35% of these patients are in an advanced stage, and nearly 10% must be considered incurable." A second cause of late diagnosis is the reluctance of some physicians to insist upon investigation when suspicious signs or symptoms exist. In New Orleans 36 patients, 60% of whom were sent to their own physicians with a Cancer Detection Clinic recommendation for further examination, received no further diagnostic procedures. If physicians take no action even after the appearance of symptoms, certainly early diagnosis is impossible.

CANCER DETECTION CLINICS

Some years ago it was recognized that neither education of the public nor even education of the medical profession would suffice if the early diagnosis of cervical cancer were to be achieved and that periodic examination of large groups of supposedly well women would have to be undertaken. In 1937 L'Esperance, and a year later MacFarlane, instituted the periodic examination of well women, and by 1948 there were already established 185 cancer detection clinics in the United States. In 1948 L'Esperance [4] reported that among 4,920 women screened during a single year (1946), 13 cases of cervical cancer (0.3%), including 8 carcinomas in situ, were found. MacFarlane,[5] in the initial examination of 1,319 women, discovered 3 cases of cervical cancer and 1 of the fundus (0.3%). A fourth case of carcinoma of the cervix was uncovered on the 11th examination of 1 of the 732 women who had been followed by a semiannual periodic check over a 10 year period. Goldman,[6] summarizing figures from several cancer detection clinics, reported 29 cervical carcinomas (none productive of obvious symptoms of disease) diagnosed in the examination of 16,241 women (0.17%). There were nine cases of cancer in situ. Skapier [7] in examinations of 10,000 women screened over a two year period, diagnosed 30 carcinomas of the cervix (0.3%), 21 of these being preinvasive. "Since January 1948," Skapier writes, "four carcinomas of the cervix (three pre-invasive) were detected among each 1,000 asymptomatic patients examined." Burns and Hartung [8] found 54 cervical cancers (0.84%) and 20 cancers of the endometrium in 6,437 women without pelvic symptoms who came to the offices of practitioners in Toledo. In 22 cases the lesion was not suspected on clinical examination. Nieburgs and Pund [9] reported the diagnosis of 185 cases of cervical carcinoma in 10,000 women screened by vaginal and cervical smears (1.85%). Of their patients with proved cancer 42% were asymptomatic; 40% of the cancers were preinvasive.

TABLE 2.—*Five Year "Cure" Rates in Stage 1 Cervical Cancer*

	Total No. of Cases at Stage 1	Relative Apparent Recovery Rate at End of Five Years, %
League of Nations *		
1913-1943		
All countries	5,655	60
American clinics	1,425	62
1939-1943		
All countries	2,362	63
American clinics	582	64
Radium Centre, Copenhagen †		
1922-1939	524	68
Radium Institute, Edinburg ‡		
1940-1944	98	70
University of Minnesota §		
1939-1947	78	80
University of California ‖		
1948	111	65

* See footnotes for table 1.

Jones [1] has recently reported 21 cervical carcinomas (0.24%) (4 preinvasive) in the examination of 8,955 women in detection centers in Maryland. Two stage 3 cancers were found in asymptomatic women. In only 10 of 21 cases did a clinical suspicion of cancer exist. It is evident that by routine examination of supposedly well women, early cervical cancer is discoverable in a significant number of cases, but it is also evident that a large variation in the incidence of detected cervical cancer appears in the reports cited above. To estimate the actual

incidence of cervical cancer in the general population is difficult. Based upon the reporting of new cases of cancer (New York State, 1945-1947) the annual incidence of carcinoma of the cervix in women between 25 and 70 years old is estimated as 40 per 100,000 (0.04%). In 10,000 unselected women then, about four new cases would be expected per year. Since there is a latent period of several years before the disease is commonly recognized, in a previously unscreened population the first screening should uncover a significantly higher number of cases than would a subsequently yearly screening of the same group. Therefore, several times the annual incidence should be disclosed on the first screening of any group of women.

TABLE 3.—*Eleven Office Patients with Positive Smears, 1946-1951*

Age	Complaint	Pelvic Examination	Biopsy	Final Pathological Report
65	Depression *	Negative	Endometrial cancer	Endometrial cancer
49	Arthritis †	Negative	Negative	Cancer in situ of cervix
62	Fatigue	Negative	Cancer in situ cervix	Cancer in situ cervix
43	Arthritis	Erosion	Cancer in situ cervix	Cancer in situ cervix
50	Cancerphobia	Polyp	Cancer in situ cervix	Cancer in situ cervix
37	Hay fever	Negative	Cancer in situ cervix	Cancer in situ cervix
47	Arthritis	Negative, retained cervix	Squamous cell cancer of cervix	Squamous cell cancer cervix, grade 2, invasive
53	Headache	Negative	Cancer in situ cervix	Cancer in situ cervix
65	Abdominal pain	Polyp	Negative	Negative
46	Chest pressure	Negative, retained cervix	Negative	Cancer in situ cervix
43	Cystitis	Cancer cervix, retained cervix	Invasive cancer of cervix, stage 1	.....

* Three weeks, leukorrhea.
† One day spotting followed administration of estrogen. All other cases were without pelvic symptoms.

Another explanation for the unexpectedly high incidence of cervical cancers detected on screening surveys was suggested by Jones and Cameron [10] who, noting that the number of cervical cancers found among women reporting to detection centers was twice the expected prevalence of the disease, concluded that the women coming to these centers did not represent an unselected group. It may be impossible to collect figures applying to a strictly unselected group. Consciously or unconsciously, investigators will often allow women with minimal symptoms to weight any series.

METHODS OF DETECTION

Initially, inspection of the cervix and biopsy of all suspicious areas were considered adequate for the exclusion of cancer. As it was learned that early malignant disease could exist in a cervix harboring an apparently innocuous lesion, or even in one completely normal in appearance, multiple biopsies and later cytological examination were included. While there is general agreement that a final diagnosis of cancer can be made only by histological examination, the relative value of biopsy and vaginal smear in the detection of early cervical cancer is still debated. Jones concludes that the smear did not add statistically to the yield of detected cancers in his group; the majority of writers find cytological examination an important asset in uncovering early disease. Kraushaar [11] writes, "(The vaginal smear's) value . . . is indicated by the high incidence of genital cancer found in the women with suspicious or positive smears. . . . Each of the three methods (cytological, clinical, and histological) alone shows a significant error rate, but by combining all three, there is an improved chance of detecting any existing genital malignancy." A similar conclusion was reached by Graham [12] and by Gates and Warren. Those who depend upon biopsy alone for the detection of early cervical cancer must admit that biopsy as a routine procedure is limited to the gynecologic clinic, that asymptomatic women do not, as a rule, go to the specialist, and finally that routine biopsies of the normal appearing cervix not infrequently fail to disclose an existing cancer.[13]

Careful screening by both biopsy and smear is discovering an increasing number of preinvasive lesions. What these lesions represent is yet another question awaiting definitive answer. Younge [14] collected from the literature 16 cases of untreated carcinoma in situ, which progressed to invasive cervical cancer, and added 2 such cases of his own. Of the experience at the Free Hospital for Women he writes, "In one deliberate and five unintentional clinical experiments carcinoma in situ has been seen to progress to invasive cancer in from eleven months to over six years." Glatthaar [15] studying "precancerous" cervical lesions, found that normal and "restless" epitheliums survive but do not grow in tissue culture; carcinoma in situ and cancer both grew actively, carcinoma in situ somewhat the more actively of the two. Glatthaar concludes that it is impossible to differentiate carcinoma in situ from true cancer by either cytological or cultural characteristics.

There have been, on the other hand, several instances of authentic carcinoma in situ, which have apparently regressed to normal. In Younge's series there are four untreated cases in which no cancer can be found by vaginal smear or biopsy one and one and one-half to two years after the original positive biopsy and definitely positive vaginal smears. Younge says that to prove that such cases have regressed is difficult "because it is theoretically possible to remove the entire lesion in one biopsy." We have noted two cases in which smears definitely positive for cancer have later become normal. In one case no biopsy was performed and the patient is under observation. In the second the cervix was sectioned, following hysterectomy, and no cancer found. Until a significantly large number of women with positive smears and normal appearing cervices can be followed for many months without operative interference, it will be impossible to estimate how often and under what conditions reversion to normal may occur. The evidence available to date points to the eventual clinical malignant behavior of most carcinomas in situ of the cervix. Whatever the final answer to this problem may be, it remains true that, if the number of women dying from cervical cancer is to be reduced, early diagnosis is essential. The detection center may be the place to find these early cases, but, more properly, it might be, as Falls [16] suggests, the

cancer were to be achieved and that periodic examination

appears in the reports cited above. To estimate the actual

physician's responsibility to discover many of these cases in his office.

In 1950 Kaufmann [17] reported examination by vaginal smear of 1,721 women coming to practioners' offices in Springfield, Mass., for general check-ups. Thirteen carcinomas of the cervix (0.8%) and 10 of the fundus were detected and histologically proven. Kraushaar reported 3 (0.24%) out of 1,238 women examined to have carcinomas of the cervix. Wachtel found 10 (1.1%) out of 946 to be afflicted. In 1948 we [18] reported the detection of 4 cases of cancer of the uterus (3 of the cervix) among 200 unselected office patients, with the use of the vaginal smear as a screening procedure. This series has now been extended to include a total of 704 women. Since January, 1946, vaginal smears have been taken routinely on almost every new female patient coming to the office of one of us (M. F-S.). In order to ascertain whether the group was weighted in the direction of pelvic disease, each new patient was asked specifically whether abnormal bleeding or discharge had been noted. Of the patients, 67 admitted leukorrhea and 29 irregular or abnormal bleeding. Thus a total of 96 (or only 13%) presented symptoms suggestive of pelvic disease.

We believe that this group of 704 represents a fair cross section of women coming to the internist for general diagnosis. Of the 704 women studied, negative smears were obtained in 693; positive or doubtful (later positive) smears in 11 cases. In one case with a positive smear, no malignant disease was found. In 10 of 11 women with positive smears, examination of fixed tissue preparations established the diagnosis of cancer (1 endometrial, 7 carcinoma in situ, and 2 invasive cancers of the cervix). This represents an incidence of 1.3% cervical cancer for the 704 women screened. In the entire group of 704, 29 had undergone previous hysterectomy. Cancer of the cervix that was retained at hysterectomy was found in three cases (10%). While the figures are too small to be statistically significant, this finding corroborates previous evidence that cancer is more common in the retained cervix than in the intact uterus.

It is interesting that the number of pelvic malignancies discovered each year by office examination remained quite constant. Thus, in 1944 (before the start of this series) three cases were found; two cases each in 1945, 1946, and 1947; none in 1948; three in 1949, one in 1950, and two cases (by October) in 1951. One case of cervical carcinoma has been uncovered in about every 100 consecutive cases in which women not previously examined are seen.

Of the seven women with carcinoma in situ and the two with invasive cancer, one admitted a single day of spotting (following estrogen given for arthritis); in eight patients no symptoms suggestive of pelvic disorder were uncovered by direct questioning. Pelvic examination of the positive group disclosed one erosion, one cervical polyp, and in one case clinical evidence of carcinoma; pelvic examination was negative in six. The two women with stage 1 carcinoma of the cervix had noted neither bleeding nor discharge. With an efficient cytological laboratory available the physician may discover carcinoma in situ in about one of every hundred new cases coming to his office. If the majority of carcinomas in situ represent lesions that will later progress to invasive cancer, office cytological examination becomes a necessary diagnostic procedure for the practicing physician.

CONCLUSIONS

Cancer of the cervix, if discovered early (international stage 1), is curable in from 70 to 80% of cases. At the present only one case in five is diagnosed in stage 1. Eighty percent of women have advanced cervical cancer when the diagnosis is made.

Early diagnosis is possible only by means of periodic examination of supposedly well women, either in detection centers or in the physician's office.

Among 704 consecutive new women patients coming to the office of an internist, pelvic cancer was detected by vaginal smear in 10 cases (1.4%).

12 Hereford St. (Dr. Fremont-Smith).

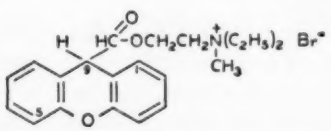
COUNCIL ON PHARMACY AND CHEMISTRY

NEW AND NONOFFICIAL REMEDIES

The following additional preparations have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

R. T. STORMONT, M.D., *Secretary.*

Methantheline Bromide. — Banthine Bromide (Searle). — β-Diethylmethylaminoethyl 9-xanthenecarboxylate bromide.—β-Diethylaminoethyl xanthene-9-carboxylate methobromide.—$C_{21}H_{26}O_3NBr$.—M.W. 420.34.—The structural formula of methantheline bromide may be represented as follows:



Actions and Uses.—Methantheline bromide, a parasympatholytic agent, produces the peripheral action of anticholinergic drugs such as atropine and the ganglionic blocking action of drugs such as tetraethylammonium chloride. Tolerated amounts of methantheline bromide exert side-effects typical of atropine-like drugs, but cause less tachycardia, and also cause less postural hypotension than does tetraethylammonium chloride. Toxic doses produce a curare-like action at the somatic neuromuscular junction.

Clinical studies indicate that the drug effectively inhibits motility of the gastrointestinal and genitourinary tracts and, to a variable degree, diminishes the volume of perspiration and salivary, gastric, and pancreatic secretions. It also decreases mucoprotein secretion. Like atropine, it produces mydriasis and cycloplegia when applied locally to the eye or administered systemically, but until more clinical evidence becomes available, its local use for this purpose is not recommended. The value of the drug for preventing abnormal cardiac reflexes through the vagus during thoracic surgery, or as an agent for routine preoperative medication in place of atropine, requires further investigation before final conclusions can be reached.

Methantheline bromide is indicated for clinical use whenever anticholinergic spasmolytic action is desired, provided it is not contraindicated because of its atropine-like characteristics or because of a patient's intolerance to the unavoidable side-effects of such therapy. It is useful as an adjunct in the management of

peptic ulcer, chronic hypertrophic gastritis, certain less specific forms of gastritis, pylorospasm, hyperemesis gravidarum, biliary dyskinesia, acute and chronic pancreatitis, hypermotility of the small intestine not associated with organic change, ileostomies, spastic colon (mucous colitis, irritable bowel), diverticulitis, ureteral and urinary bladder spasm, hyperhidrosis or control of normal sweating which aggravates certain dermatoses, and control of salivation.

Methantheline bromide produces some degree of cycloplegia and mydriasis in therapeutic doses and therefore should not be administered to patients with glaucoma. It sometimes decreases the ability to read fine print. Xerostomia (dryness of the mouth) is a common, sometimes transient, side-effect. Urinary retention of varying degrees may occur in elderly male patients with prostatic hypertrophy, and some patients may have difficulty emptying the rectum. Patients with edematous duodenal ulceration may experience nausea and vomiting during initial administration of the drug. These patients should take only liquids during the institution of drug therapy. All patients should be advised of the possible occurrence of side-effects. Overdosage sufficient to produce a curare-like action may be counteracted by prompt subcutaneous injection of 2 mg. of neostigmine methylsulfate.

Dosage.—Methantheline bromide is administered orally or parenterally by either the intramuscular or intravenous route. Parenteral administration is not advised for patients able to take the drug orally. The average initial dose for adults, oral or parenteral, is 50 mg. For patients with considerable intolerance, 25 mg. may be employed. In the management of peptic ulcer, a beginning schedule of 50 mg. three times daily before meals, and 100 to 150 mg. on retiring is suggested. However, the usual effective dose is 100 mg. four times daily, although some patients may require more or less than this amount. The dosage may be increased to tolerance, using dryness of the mouth as a guide, and adjusted to meet the individual response of patients. Maintenance dosage in peptic ulcer is usually considered to be about one-half the therapeutic level. In the management of other hypermotile or hypersecretory states, the dosage should be adjusted to the smallest amount which will relieve the symptoms. When spastic conditions are secondary to inflammatory or other organic lesions, therapy directed toward the cause should be employed whenever possible.

Tests and Standards.—

Physical Properties: Methantheline bromide is a white or nearly white, odorless, micro-crystalline powder with a very bitter taste. It melts between 172 and 177°. It is very soluble in water, freely soluble in alcohol, and practically insoluble in ether. A 2% solution has a pH between 5.0 and 5.5.

Identity Tests: Dissolve about 0.25 gm. of methantheline bromide in 10 ml. of water. To 2 ml. of the solution add 5 ml. of water, 2 ml. of diluted nitric acid and 2 ml. of silver nitrate T.S.: a light yellow, curdy precipitate forms which is only slightly soluble in ammonia T.S. (*presence of bromide*). To the remainder of the solution add 5 ml. of 10% sodium hydroxide and heat carefully to boiling. Keep the mixture hot for about 2 min., cool slightly and acidify with about 5 ml. of 5 *N* hydrochloric acid. Swirl to coagulate the precipitate, allow the mixture to cool and filter it. Wash the precipitate thoroughly with water and dry it at 105° for 1 hour: the white solid melts between 218 and 223°.

To about 10 mg. of methantheline bromide in a test tube, add 5 ml. of sulfuric acid: a bright yellow to orange solution is obtained.

A 0.005% solution of methantheline bromide in alcohol, prepared as directed in the spectrophotometric assay, exhibits ultraviolet absorption maxima at about 2460 Å [E(1%,1 cm.), about 135] and 2820 Å [E(1%,1 cm.), about 69], and minima at about 2400 and 2700 Å. The ratio of the absorbancies at 2460 and 2820 Å is between 1.85 and 2.05.

Purity Tests: Dry about 2 gm. of methantheline bromide in a vacuum desiccator over phosphorus pentoxide for 24 hours: the loss in weight is not more than 0.5%.

Char about 1 gm. of methantheline bromide, accurately weighed, over a low flame. Cool the charred mass, then add 1 ml. of sulfuric acid and continue ignition until no carbon remains: the amount of residue present is not more than 0.1%.

Assay: (Methantheline) Transfer about 0.1 gm. of methantheline bromide, accurately weighed, to a 100 ml. volumetric flask and fill to the mark with alcohol. Mix thoroughly and transfer exactly 5 ml. to a second 100 ml. volumetric flask, fill to the mark with alcohol and mix thoroughly. Determine the absorbancy of the final solution (0.005%) at 2820 Å with a spectrophotometer. The number of mg. of methantheline bromide per ml. of the final solution = absorbancy ÷ 6.9. The amount of methantheline bromide present is not less than 96.5 nor more than 103.0%.

(Bromide) Transfer about 0.5 gm. of methantheline bromide, accurately weighed, to a 250 ml. Erlenmeyer flask. Dissolve it in about 30 ml. of water and add 10 ml. of diluted nitric acid. Add exactly 20 ml. of 0.1 *N* silver nitrate, stir well and filter the mixture through a sintered glass funnel. Wash the precipitate with three 10 ml. portions of 2% nitric acid and combine the washings with the filtrate. To the filtrate add 2 ml. of ferric ammonium sulfate T.S. and titrate the excess silver nitrate with 0.1 *N* ammonium thiocyanate. Each ml. of 0.1 *N* silver nitrate used is equivalent to 0.007992 gm. of bromide and 0.04203 gm. of methantheline bromide. The amount of bromide present is not less than 18.4 nor more than 19.2%, equivalent to not less than 96.8 nor more than 101.0% of methantheline.

(Nitrogen) Transfer to a semi-micro Kjeldahl flask about 0.15 gm. of methantheline bromide. Digest it for 4 hours with 7 ml. of sulfuric acid, 2.7 gm. of potassium sulfate and 0.3 gm. of mercuric oxide. Cool the contents of the flask and carefully add 15 ml. of water. Make the solution alkaline with 40% sodium hydroxide and then add 10 ml. of 40% sodium thiosulfate. Distil the ammonia into 20 ml. of 4% boric acid. Using a mixed indicator (1:5 methyl red T.S. and bromocresol green T.S.), titrate the ammonia liberated with 0.05 *N* sulfuric acid. Each milliliter of 0.05 *N* acid is equivalent to 0.0007004 gm. of nitrogen and 0.02102 gm. of methantheline bromide. The amount of nitrogen present is not less than 3.28 nor more than 3.40%, equivalent to not less than 98.5 nor more than 102.0% of methantheline bromide.

Dosage Forms of Methantheline Bromide

TABLETS. *Identity Tests:* Powder enough tablets to give about 0.5 gm. of methantheline bromide and triturate the material with about 20 ml. of alcohol. Filter the mixture and evaporate the filtrate on a steam bath. The residue responds to the identity tests listed in the monograph for Methantheline Bromide.

Assay: (Methantheline) Powder 10 tablets and transfer to a 100 ml. volumetric flask an amount, accurately weighed, equivalent to about 0.1 gm. of methantheline bromide. Add about 50 ml. of alcohol and mix thoroughly. Fill to the mark with alcohol and again mix thoroughly. Allow the suspension to settle and transfer exactly 5 ml. of the supernatant solution to a second 100 ml. volumetric flask. Proceed as directed in the spectrophotometric assay in the monograph for Methantheline Bromide starting with, "Determine the absorbancy . . ." The amount of methantheline bromide present is not less than 95.0 nor more than 105.0%.

(Bromide) Powder 20 tablets and transfer to a 100 ml. volumetric flask an amount, accurately weighed, equivalent to about 0.5 gm. of methantheline bromide. Add 5 ml. of alcohol and then fill the flask about half full with water. Shake thoroughly, fill to the mark with water and again mix thoroughly. Allow the suspension to settle and filter the supernatant liquid, discarding the first 20 ml. of filtrate. Transfer exactly 50 ml. of the subsequent filtrate to a 250 ml. Erlenmeyer flask, add 5 ml. of 5 *N* nitric acid and exactly 10 ml. of 0.1 *N* silver nitrate. Swirl to coagulate the precipitate and add about 0.1 gm. of decolorizing charcoal. Filter the solution through a sintered glass funnel. Wash the precipitate with three 10 ml. portions of nitric acid and combine the washings and filtrate. To the filtrate add 2 ml. of ferric ammonium sulfate T.S. and titrate the excess silver nitrate with 0.1 *N* ammonium thiocyanate. Each ml. of 0.1 *N* silver nitrate used is equivalent to 0.007992 gm. of bromide and 0.04203 gm. of methantheline bromide. The amount of methantheline bromide present is not less than 95.0 nor more than 105.0% of the labeled amount.

POWDER. *Identity Tests:* Combine the contents of enough ampuls to yield about 0.3 gm. of methantheline bromide. The powder responds to the identity tests listed in the monograph for Methantheline Bromide.

Assay: (Methantheline) Using alcohol as the solvent, quantitatively transfer to a 50 ml. volumetric flask the contents of enough ampuls to give about 0.25 gm. of methantheline bromide. Fill to the mark with alcohol and mix thoroughly. Transfer to a 100 ml. volumetric flask exactly 20 ml. of this solution and fill to the mark with alcohol. Proceed as directed in the spectrophotometric assay in the monograph for Methantheline Bromide starting with, "Mix thoroughly and transfer . . ." The amount of methantheline bromide present is not less than 93.5 nor more than 106.5% of the labeled amount.

(Bromide) Using about 30 ml. of water as the solvent, quantitatively transfer to a flask the contents of enough ampuls to yield about 0.5 gm. of methantheline bromide. Proceed as directed in the assay for bromide in the monograph for Methantheline Bromide starting with, ". . . add 10 ml. of diluted nitric acid." The amount of methantheline bromide present is not less than 93.5 nor more than 106.5% of the labeled amount.

G. D. Searle & Company, Chicago

Powder Banthine Bromide: 5 cc. ampuls. 50 mg.

Tablets Banthine Bromide: 50 mg. U. S. Trademark 537,763.

Neostigmine Methylsulfate-U.S.P. (See New and Nonofficial Remedies 1952, p. 174).

The Vitarine Company, Inc., New York.

Solution Neostigmine Methylsulfate: 5 cc. vials. A solution containing 1 mg. of neostigmine methylsulfate in each cubic centimeter. 1 cc. ampuls and 10 cc. vials. A solution containing 0.5 mg. of neostigmine methylsulfate in each cubic centimeter. Preserved with 0.18% methylparaben and 0.02% propylparaben.

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ANOTHER PREMATURELY PUBLICIZED DRUG

With the appearance on the newsstands of the November issue of one of the popular pocket magazines, physicians throughout the country will be besieged by patients demanding a new drug called "betasyamine," reportedly a combination of betaine and glycocyamine. This preparation, described in a sensational article as a "miracle drug . . . ready to take its place side by side with those other 'miracle drugs,' insulin, the sulfa compounds and penicillin," has, according to the article, proved dramatically successful in the treatment of heart disease (type unspecified), rheumatoid arthritis and the paralysis resulting from poliomyelitis. This drug, it is stated, "will soon be available to the general public under medical supervision."

Physicians will be interested to know that published clinical data on these compounds are extremely limited. The originators of the treatment have published reports of its use in a total of 35 patients with cardiac decompensation [1] and 31 patients with paralysis following poliomyelitis.[2] They have apparently published no results of its use in arthritis. In none of the studies published in scientific journals have they used untreated controls or comparable groups of patients treated with placeboes or other medication. In contrast to the good results reported by these investigators and the popular article are the largely negative results obtained by other workers. Graybiel and Patterson [3] state: "In our experience betaine and glycocyamine were of little value in the relief of congestive failure in decreasing cardiac enlargement and in abolishing the electrocardiographic pattern of left ventricular strain. In some instances work tolerance as measured by a modification of the 'Harvard step test' increased but the increase was usually small and sometimes was not maintained. In some cases where subjective improvement led to an increase in the patients' activities, there was evidence that the heart was overworked." Higgins and others [4] state: "Under the conditions of the study here reported, no significant advantage has been shown to result from oral administration of glycocyamine and betaine to patients with arthritis of various types." The writer of the article on "betasyamine" apparently overlooked these nonconfirmatory results.

Physicians should also note that the safety of these drugs in the doses used has not been certified by the federal Food and Drug Administration, so that they are available only for experimental use. There is evidence that glycocyamine taken alone without betaine is capable of producing urinary obstruction, and the two drugs in combination have been reported to produce transitory hypoglycemia, although Higgins failed to confirm this observation. Whether other immediate or delayed reactions will appear in larger series of patients is not known. Evidence of the therapeutic efficacy of these compounds has not yet been evaluated by the Council on Pharmacy and Chemistry of the American Medical Association.

As a result of the article mentioned, many desperately ill or discouraged patients will again have their hopes prematurely and perhaps falsely raised by the recommendation of an unproved drug by a lay writer. Urgently needed standard therapy may be postponed or neglected by patients in the hope of obtaining a new drug not yet available in interstate commerce. This incident is not an isolated one. The premature release of inadequately confirmed medical information and the "prescription" of drugs, diets, or surgical procedure for specific diseases by lay publications is a common phenomenon in American periodical literature. It is to be hoped that the consciences of science writers, publishers, and pharmaceutical houses will limit such abuses in the future.

1. Borsook, M. E., and Borsook, H.: Treatment of Cardiac Decompensation with Betaine and Glycocyamine, Ann. West. Med. & Surg. 5: 830 (Oct.) 1951. Van Zandt, V., and Borsook, H.: New Biochemical Approach to the Treatment of Congestive Heart Failure, ibid. 5: 856 (Oct.) 1951.

2. Borsook, M. E.; Billig, H. K., and Golseth, J. G.: Betaine and Glycocyamine in the Treatment of Disability Resulting from Acute Anterior Poliomyelitis, Ann. West. Med. & Surg. 6: 423 (July) 1952.

3. Graybiel, A., and Patterson, C. A.: Use of Betaine and Glycocyamine in the Treatment of Patients with Heart Disease: Preliminary Report, Ann. West. Med. & Surg. 5: 863 (Oct.) 1951.

4. Higgins, A. R., and others: Effects of Creatine Precursors in Arthritis: Clinical and Metabolic Study of Glycocyamine and Betaine, California Med. 77: 14 (July) 1952.

EMPLOYMENT OF THE HANDICAPPED

Oct. 11 marks the end of National Employ the Physically Handicapped Week. While most physicians realize that handicapped persons properly trained and selectively placed become valuable employees capable of working as regularly, productively, and safely as those without handicap, there is a tendency to consider the problem as one of primary concern to industry and social workers. In reality, this problem is of immediate professional and economic importance to physicians. The employability of a patient after injury or illness or in the presence of a congenital defect often depends as much on the skill and thoroughness exercised in his rehabilitation as on the extent of his initial injury or defect. Such rehabilitation is the direct responsibility of the physician. The emphasis that has been placed in medical education on the management of the acute phase of an injury or illness often tends to obscure the importance of the long and tedious process of restoration of function by means of physical therapy, muscle or sensory reeducation, use of prostheses, or similar procedures. The practice of assisting a patient through the emergency phase of his disability and then neglecting the phase of rehabilitation is the equivalent of rescuing a drowning man only to abandon him on a desert island. Physicians who do not have the time or training to carry out rehabilitation programs are obligated to refer their patients to qualified personnel in this field.

Rehabilitation programs are rewarding not only from the humane but from the economic standpoint as well. A survey [1] by the Task Force on the Handicapped, Office of Defense Mobilization, under the chairmanship of Dr. Theodore G. Klumpp brings out this point clearly: "There are thousands of people [both potential wage earners and their dependents] who are receiving public assistance today, as well as other aid from public and private sources, whose economic plight stems directly from a physical disability. Provided with rehabilitation, many of them will leave the public aid rolls and become self-supporting again. . . . Cutting down the drain on municipal, state and federal expenses can save this country untold millions of dollars. Yet this is only one side of the coin. Restoring these men and women to the status of wage earners creates tax payers. It has been shown quite clearly that among the handicapped persons rehabilitated in the federal-state vocational rehabilitation programs, $10 in federal taxes are returned to the government for every federal dollar spent for rehabilitation. And this, of course, takes no account of the tax yield to states and municipalities." Estimates of the prevalence of disability quoted in the report of the task force give some idea of the magnitude of the problem. It has been calculated that as many as 28 million Americans have some chronic disease, orthopedic impairment, or serious defect of vision or hearing. Although many of these persons are unemployable for reasons of age or total disability, and some are already employed, it has been estimated that there remain 2 million disabled persons in this country who could and should be rehabilitated and placed in employment or in more productive jobs. An additional 250,000 persons become disabled annually. This represents a significant burden on the taxpayer and a significant manpower deficit in these days of labor shortages and partial mobilization.

Physicians aware of the importance to their patients and to themselves of employment of the handicapped can take an active part in promoting such employment in their own communities. A program that might be followed is outlined in the report of the Task Force on the Handicapped, which can be obtained from the Government Printing Office, Washington 25, D. C. This program includes (1) formation of a community promotional organization, (2) a survey of the extent of the problem and the personnel and facilities available for its solution, (3) the organization of a rehabilitation team consisting of a physician, physical therapist, vocational rehabilitation specialist, state employment service representative, and local industrial personnel directors to screen disabled persons and supervise their rehabilitation, (4) the recommendation to personnel departments of industries and businesses that they examine their hiring policies with the idea of establishing specific physical standards for each job, which might permit the hiring of the handicapped for some jobs, rather than blanket requirements for all jobs, which usually exclude handicapped persons entirely, (5) the maintenance of lists of available handicapped workers for employers, (6) development of on-the-job training for the handicapped, (7) recommendation that employers experiencing difficulty in obtaining enough workers locally consider hiring qualified handicapped workers before recruiting from outside areas, and (8) recruitment of new students in physical therapy, occupational therapy, psychology, rehabilitation counselling, social work, and other fields essential to complete rehabilitation. At the state level the report recommends that workmen's compensation laws be altered so as not to impede the hiring of the handicapped or delay referral of the injured for rehabilitation. The encouragement of increased emphasis on physical medicine and rehabilitation in medical education might also be of value. Physicians should regard participation in this broad program as an obligation and a privilege.

PHYSIOLOGICAL LIMITS FOR RUNNING

Although man has been running foot races for thousands of years, it is only within the past century that clocking devices have made it possible to record his running time accurately. With some 75 years of clocked competition now registered, it is increasingly difficult for an athlete to place his name in the record book. Recently, Lietzke [1] made an analysis of running records most likely to be surpassed and by how much, by plotting curves on the basis of the best human performance at various distances from 100 yards to 25 miles. Performances were considered in terms of average speed over a full distance, rather than the total time for a race. A smooth curve was drawn through the best world records, with points on the curve presumably representing the limit, or very close to the limit, of track athletes' possible achievements at each given distance. From these curves it was calculated that the world's record for 100 meters should be surpassed by men by 0.1 second; for 200 meters, by 0.2 second; for 1,000 meters, by 3.1 seconds; for 20,000 meters, by 46.3 seconds; for 880 yards, by 1.9 seconds; for 2 miles, by 3.3 seconds; for 3 miles, by 5.9 seconds; for 6 miles, by 30.1 seconds; and for 10 miles, by 21 seconds.

When world-record times for various distances were plotted against average speeds represented by these times, a curve was derived from which Lietzke drew a number of conclusions. The maximum in the curve occurred at 15 seconds, with the best average speed for the time being 0.00630 mile per second. This corresponded to a distance of about 150 meters, which apparently is the optimum distance for man to run if he wishes to achieve the maximum rate. Since this distance provides a runner with the opportunity to prove his maximum rate of speed, it would seem a more logical race than the standard 100 and 200 meter events.

Analysis of women's track records supplied identical conclusions, namely, that women should be able to run faster than their current track records indicate. Women runners, for example, should be able to cut 0.1 second from the 100 yard dash record; 0.3 second from the 220 yard dash; and 1.5 seconds from the best time for 800 yards. In a world calling for more and more speed, this study suggests that men and women alike have not yet attained the physiological limits for running foot races.

1. Report of the Task Force on the Handicapped to the Chairman, Manpower Policy Committee, Office of Defense Mobilization, Jan. 25, 1952.

1. Lietzke, M. H.: Running Records, Scient. Am. 187: 52 (Aug.) 1952.

ORGANIZATION SECTION

FEDERAL MEDICAL LEGISLATION SUMMARY

The 82nd Congress convened Jan. 3, 1951, and adjourned sine die, July 7, 1952. During this period approximately 14,000 legislative measures were introduced in the Senate and House. Of these, 250 were of sufficient medical significance to be followed by the Washington Office of the American Medical Association, and the chief points are briefly summarized below.

Bills That Became Law

Numerically, the commonest measures of interest to the medical profession as such were those dealing with research and aid programs. Of the 54 such measures, only one became law (Public Law 579, introduced by Congressman Buckley). It extended the duration of the Water Pollution Control Act three additional years and authorized federal assistance to states through studies, loans, and grants. The authorized grants amounted to one million dollars annually; however, no appropriation was voted. Of the 44 military and defense measures followed by the Washington Office, 6 became public laws. Originally introduced by Senator Johnson of Texas, S. 1 became Public Law 51, June 19, 1951. This amends the Selective Service Act and establishes a commission for studying universal military training and extends the period of service required under the Doctor-Draft law from 21 to 24 months.

Senator Maybank introduced a measure to provide for defense housing and community facilities. This became Public Law 139, Sept. 1, 1951, and provides among other things for the authorization of loans and grants for construction of hospitals in defense-impacted areas. No hospital grants have been made under this law. Public Law 531, effective June 14, 1952, was sponsored also by Senator Maybank and amends the defense housing and community facilities law authorizing additional expenditures of funds for community facilities in critical defense areas, including hospitals, sewage disposal, and water purification. To date, $2,500,000 has been allocated under this program for sewage disposal and water purification.

Senator Hunt introduced two measures that became laws (Public Laws 408 and 410). Both became effective June 25, 1952. The former provides for the appointment of women physicians and specialists for medical service in the armed forces. The latter extends the special $100 monthly incentive pay for military physicians and dentists, including the commissioned corps of the U. S. Public Health Service.

The laws pertaining to the reserve components of the military service were rewritten in Public Law 476, effective July 9, 1952, in a measure introduced by Congressman Brooks. This act places in the statute many of the regulations concerning reservists, fixes more definitely the rights and responsibilities of the members of the various branches of the reserve, and provides that the armed services will establish a promotion policy providing for attrition of those who fail to advance in grade.

Of the 25 Social Security measures, 2 became public laws. The Jenner amendment to the tax bill became a part of Public Law 183. This permits limited disclosure of the names of public assistance recipients but prohibits the use of these names for political or congressional purposes. Congressman Doughton introduced in the closing part of the session H. R. 7800, an amendment to the Social Security Act to increase benefits and to preserve the rights of totally and permanently disabled persons. This became Public Law 590, July 18, 1952, but the waiver of premiums for total and permanent disability does not become effective without further action taken prior to June 30, 1953, when the disability provision expires.

Two of the 24 proposed veterans measures were enacted, one was signed by the President, and the other passed over his veto. Senator Jenner sponsored Public Law 28, effective May 11, 1951, providing medical, hospital, compensation, and pension benefits for Korean veterans, similar to benefits for veterans of World War II. The President vetoed H. R. 3193, introduced by Congressman Rankin, but Congress overruled his veto, and this became Public Law 149, Sept. 18, 1951, and provides for $100 monthly benefits to veterans with non-service-connected disabilities who need full-time attendants at home.

Twelve measures dealing with drugs were introduced. Of these, only H. R. 3298, by Congressman Durham, passed. It became Public Law 215, Oct. 26, 1951. This amends the Federal Food, Drug, and Cosmetic Act defining prescription drugs by statute and requires the manufacturer to use a caution label on poisonous drugs; it legalizes prescriptions by telephone from licensed practitioners and allows pharmacists to refill prescriptions for non-dangerous drugs without a second prescription.

Other Measures, None of Which Became Law

Of the bills introduced that never became law, there were 18 measures for federal aid to medical education, 13 for child health and school programs, 12 involving hospitals, 10 for tax deductions for medical bills and insurance, 8 for health programs, including health insurance, 7 for reorganization of the executive departments of government, 6 for local public health subsidies, 4 for federal employee health programs, and 3 for industrial safety.

Important measures that passed only one House of Congress and were not enacted into law were S. 445 and H. J. Res. 218. S. 445, concerning local public health units, introduced by Senator Hill and passed by the Senate. A companion bill, H. R. 274, introduced by Congressman Priest, was considered by the House Interstate and Foreign Commerce Committee. Hearings were held, but no action was taken. H. J. Res. 218, introduced by Congressman Murphy, provided for air pollution research, passed the House July 2, 1952, and was reported in the Senate July 3, 1952.

Unless the 82nd Congress is recalled in special session prior to Jan. 3, 1953, when the 83rd Congress convenes, all measures introduced in the 82nd Congress, but not passed, will die.

ANNUAL CONFERENCE OF WOMAN'S AUXILIARY

The ninth annual conference of state presidents, presidents-elect, and national committee chairmen will be held at the Hotel LaSalle, Chicago, Nov. 6-7. The theme of the conference will be "Our Goal . . . A Better World." Among other things, the agenda includes a report of the president, an address by Dr. Ernest B. Howard, Assistant Secretary of the American Medical Association, panels on organization, program, nurse recruitment, civil defense, *Today's Health*, American Medical Education Foundation, public relations and community service, legislation, and question and answer periods. At the luncheon on Thursday, Arthur L. Conrad, president of the Heritage Foundation, will speak on "The Meaning of Education in the Modern World," and, at the luncheon on Friday, Mrs. Oscar Ahlgren, president, General Federation of Women's Clubs, will speak on "The Time Has Come." Representatives of the various state auxiliaries will take part in the panel discussions, while others have been assigned to speak on such subjects as The World Medical Association, The Mechanics of a Convention, Auxiliary Finances, The History of the National Auxiliary, The Speakers' Bureau, and Blue Cross and Blue Shield. At 2 p. m. Friday, a Community Play of the American Theatre Wing, "Scattered Showers," will be presented by three Woman's Auxiliary leaders, and, at 3 p. m. Friday, guides will conduct a tour through the American Medical Association headquarters building at 535 N. Dearborn St.

PORTRAIT OF DR. WEST

Mr. Oskar Gross, Chicago, portrait artist, has been commissioned by a committee representing a large group of A. M. A. employees to paint an oil portrait of the late Dr. Olin West, who served many years as Secretary and General Manager of the American Medical Association. The committee already has secured voluntary employee contributions amounting to half the cost of the portrait. It is planned to hang the picture in the secretary's office at A. M. A. headquarters.

MEDICAL NEWS

ARIZONA

Hearing Tests in Schools.—According to the Arizona State Department of Health, hearing losses were discovered in 188 (3.25%) of 5,781 school children tested in 17 schools during the first half of 1952. School authorities already have placed requests for testing programs at Nogales, Gilbert, Holbrook, Pinal County, and in Phoenix at Wilson, Osborn, Roosevelt Third Street, Alhambra, and St. Francis Xavier schools. The program is available to all schools.

CALIFORNIA

Cardiac Symposium.—The Los Angeles County Heart Association will hold symposiums on pharmacology, hypertension, and peripheral vascular disease, at the Wilshire-Ebell Theater, 4401 W. 8th St., Los Angeles, Oct. 15 and 16. The guest speakers will include: Drs. C. Sidney Burwell, Boston, Julius H. Comroe Jr., Philadelphia, Keith S. Grimson, Durham, N. C., Robert L. King, Seattle, Harry Mandelbaum, New York, and Maurice L. Tainter, Albany, N. Y.

CONNECTICUT

Hospital-Medical Education Day.—The Hartford County Medical Association will sponsor its first Hospital-Medical Education Day Oct. 27 in cooperation with the Parent-Teacher Association and St. Francis, Mt. Sinai, and Hartford hospitals. Members of Greater Hartford's 15 PTA councils will be conducted on tours of the three hospitals as part of the day's activities. Preceding the tours, representatives of the Hartford County Medical Association will speak briefly on medical education and training and the responsibilities that physicians assume in caring for their patients. A question and answer period will follow.

FLORIDA

Cardiac Physiology Course.—The National Children's Cardiac Home, Miami, is sponsoring a course in cardiac physiology, Oct. 20-23, from 5:30 to 7:30 p. m. The guest lecturers are Dr. Richard Bing, University of Alabama, Birmingham, and Dr. James V. Warren, Duke University School of Medicine, Durham, N. C. Registration is now open; the fee is $15.

ILLINOIS

Meeting of General Practitioners.—The Illinois Academy of General Practice will hold its annual scientific assembly Oct. 21-23 at the Pere Marquette Hotel, Peoria, under the presidency of Dr. Carleton R. Smith, Peoria. Speakers will include:

Edward L. Compere, Chicago, Backache.
Edward F. Rosenberg, Chicago, Medical Treatment of Arthritides.
Daniel L. Sexton, St. Louis, Office Endocrinology.
Charles J. Smith, Chicago, Traumatic Occurrences Associated with the Female Genital Tract.
Arthur P. Klotz, Chicago, Liver Tests and the General Practitioner.
Aldo A. Luisada, Chicago, Present Status of Coronary Disease—Its Diagnosis, Prognosis and Management.
Lowell T. Coggeshall, Chicago, Changes in the Past Decade in the Treatment of Medical and Surgical Diseases.
Eugene L. Jackson, Ph.D., Richmond, Va., Pharmacology as Related to Medical Practice.
Walter J. Reich, Chicago, Office Gynecology.
William M. Lees, Chicago, Trends in Surgical Treatment of Pulmonary Tuberculosis.
Clifford J. Barborka, Chicago, Nutrition in Health and Disease.
Mr. William A. Richardson, Rutherford, N. J., Doctor-Patient Relationship and Doctor-Hospital Relationship.
Robert W. Keaton, Chicago, Office Management of Diabetes.
Clement L. Martin, Chicago, Office Proctology.

The annual banquet will be in the Grand Ballroom at 7 p. m. Wednesday. Mr. Lester O. Schriver, National Freedom Foundation winner, will speak on "Living in Tomorrow's World."

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

Chicago

Hospital News.—Dr. Rachmiel Levine, director, department of metabolic and endocrine research, Michael Reese Hospital, has been appointed to the newly established position of full time chairman of the department of medicine and director of the hospital's educational program. His new duties, which he will assume Oct. 15, will involve the further development of an integrated training program for interns and residents. Dr. Levine has been associated with Michael Reese Hospital since 1935.

Gynecologic Society Meeting.—The Chicago Gynecological Society will meet at the Knickerbocker Hotel (telephone SUperior 7-4264), Oct. 17 at 8 p. m., when Dr. Nicholson J. Eastman, Baltimore, will deliver the annual Joseph L. Baer lecture on "Premature Spontaneous Rupture of the Membranes: Its Bearing on Maternal and Fetal Outlook." The clinical meeting of the society will be at Mercy Hospital, 2537 Prairie Ave., Friday. The morning session will be devoted to demonstration of gynecologic surgery by the departmental staff. In the afternoon the following presentations will be made:

John H. Isaacs, Review of Our Experience in Placenta Previa.
Charles J. Smith, Survey of Prolonged Labor Service.
Clyde J. Geiger, Statistical Analysis of Activities of Tumor Clinic at Cook County Hospital.
Herbert E. Schmitz, Analysis of the End-Results of Pelvic Exenteration.

INDIANA

Cancer Research Unit.—Contracts have been awarded for construction of a $521,000 cancer research unit at Indiana University Medical Center, Indianapolis. The unit will be built as a wing of the James Whitcomb Riley Hospital for Children. A grant of $126,000 for construction was made by the U. S. Public Health Service. Completion of the center's $4,500,000 Student Union-Hospital Food Service Building is expected by the middle of next year.

Personal.—Dr. F. R. Nicholas Carter, secretary, South Bend Board of Public Health, and city health officer, was honored at the annual meeting of the Indiana Public Health Association in Indianapolis, where he was given a citation for "distinguished and effective service in the field of public health."——Dr. Charles Myers, former superintendent of Indianapolis General Hospital, has been named to the board charged with administration of the new, combined city and county health departments. Dr. Myers currently is president of the city board of health as now constituted.

KANSAS

Fluoridation of Water Supply.—Garnett, Seneca, and Fort Scott have increased to six the number of cities in Kansas that have adjusted the fluoride content of the public water supply. The program has been approved by 12 additional cities in Kansas.

No Traffic Deaths in Fifteen Kansas Cities.—The National Safety Council lists the following Kansas cities as having no traffic deaths during 1951 and only a few for a longer period: cities of from 10,000 to 25,000 population, Winfield, four years; Manhattan, three years; Leavenworth, two years; Ottawa, two years; and El Dorado, Emporia, and Pittsburg, one year each. Cities of from 5,000 to 10,000 population that had no traffic deaths during 1951 include the following: Concordia, Hays, Iola, Liberal, McPherson, Olathe, Pratt, and Wellington. None of the larger Kansas cities went without a traffic fatality.

MASSACHUSETTS

Society News.—The Springfield Academy of Medicine will hold a joint meeting with the Western Chapter of the Massachusetts Heart Association Oct. 14. Dr. Herman K. Hellerstein, chief of the cardiac classification work unit at the Cleveland Heart Clinic, will speak on "Cardiac Work Classification Unit."

University News.—Dr. Paul C. Zamecnik has been appointed to the permanent teaching and research staff of Harvard Medical School, Boston, as associate professor of medicine at the Massachusetts General Hospital. Dr. Zamecnik has been conducting investigations in the chemistry of cancer and other malignant growths. He has twice won the John Collins Warren Triennial Prize given by the hospital for outstanding medical essays.

MICHIGAN

Annual Cancer Research Meeting.—The Detroit Institute of Cancer Research will hold its annual meeting at the Horace H. Rackham Educational Memorial, 100 Farnsworth Ave., Oct. 20-22. The clinical program, Wednesday afternoon, sponsored by the American Cancer Society, Southeastern Michigan Division, will be as follows:

Localization and Treatment of Gliomas of the Brain, Loyal Davis, Chicago.
Appraisal of Radioisotopes in Cancer Therapy, Shields Warren, Boston.
Problem of Pigmented Moles and Malignant Melanoma, George T. Pack, New York.
Recent Experience in the Chemotherapy of Cancer, Sidney Farber, Boston.

Other topics to be discussed during the sessions include:

Biochemical Mechanisms in Insect Growth and Metamorphosis, Carroll M. Williams, Boston.
The Problem of Autonomy and Dependence of Tumor Cells, Jacob Furth, Oak Ridge, Tenn.

MISSISSIPPI

Hospital Association Convention.—The 21st annual meeting of the Mississippi Hospital Association will be held in Jackson Oct. 15-17, under the presidency of Dr. Aubrey V. Beacham, Magnolia, who is also a councilor in the state medical association.

New Medical School.—Bids for the construction of the new four year medical school and the 350 bed teaching hospital at Jackson are being received by the architects for formal consideration Oct. 15. Since the plans and specifications have complete approval and the necessary $8,500,000 are committed and available, it is expected that construction will begin during November.

NEW JERSEY

Society News.—At a recent meeting in Newark, the New Jersey Dermatological Society elected Dr. Eva T. Brodkin, Newark, president; Dr. Cedric C. Carpenter, Summit, vice-president; Dr. Frederick C. Licks, South Orange, secretary; and Dr. Harry C. Goldberg, Plainfield, treasurer.

Program on Epilepsy.—The New Jersey Neuropsychiatric Association and the New Jersey Society for Crippled Children and Adults are sponsoring a program on epilepsy to be held at the Newark Academy of Medicine Oct. 15. At 3 p. m. there will be a panel discussion on rehabilitation of the epileptic patient. The evening session will include a demonstration of electroencephalography and typical records, a film "Seizure," produced by the Veterans Administration, and short talks on what is being done for the epileptic patient in New Jersey, facilities for treatment, the value of the electroencephalograph, new drug and electric therapies, and what can be done about prejudice. The meeting is open to the medical and allied professions.

Orthopedic Program.—The New Jersey Orthopaedic Society is sponsoring a program at the Kessler Institute for Rehabilitation, West Orange, Oct. 11. Dr. Robert Brendze will speak on Judet arthroplasty, and Dr. Ludwig Guttmann, director of the Spinal Injuries Centre, Stoke Mandeville, England, will discuss rehabilitation of the paraplegic. Discussion periods and an executive session of the New Jersey Orthopaedic Society will conclude the morning program. After luncheon Dr. Douglas P. Murphy, University of Pennsylvania, will speak on statistical aspects of congenital defects, Leslie C. Dunn, Sc.D., Columbia University, on the genetic aspects, and Dr. Robert F. Korns, New York State Department of Health, on the epidemiological aspects. A clinic on congenital defects will also be held.

NEW YORK

Seventh District Branch Meeting.—The annual meeting of the Seventh District Branch of the Medical Society of the State of New York will be held Oct. 15 at the Sampson Air Force Base on Seneca Lake near Geneva. At 10:30 a. m. there will be a panel discussion on the public relations and medical economic aspects of the practice of medicine, with Dr. Floyd S. Winslow, Rochester, as moderator.

Hospital News.—The new 617 bed medical-surgical building at Buffalo State Hospital will be dedicated Oct. 14. The building was erected at a cost of $4,747,000 under the state's $178,000,000 construction program, which will provide some 14,000 new beds in 17 institutions. It is the second of several similar buildings provided for in the current building program of the Department of Mental Hygiene. The first to be completed was a 960 bed facility at Hudson River State Hospital, Poughkeepsie. Nearing completion are a 768 bed medical-surgical building at Binghamton State Hospital and a similar facility for 718 patients at Utica State Hospital. Other medical-surgical buildings in various stages of planning include a 1,200 bed unit for Manhattan State Hospital and a 1,030 bed unit for Rochester State Hospital. A comparatively recent innovation in mental hospital planning, the medical-surgical buildings concentrate medical, surgical, and diagnostic facilities under one roof.

New York City

Harvey Lectures.—James F. Bonner, Ph.D., professor of biology, California Institute of Technology, Pasadena, will deliver the first Harvey lecture of the current series at the New York Academy of Medicine, Oct. 23, on "The Hormonal Control of Plant Growth."

Dr. Co-Tui Honored.—Dr. Frank W. Co-Tui, member of the psychiatric research staff of the Creedmoor Institute for Psychobiologic Studies, on a recent visit to the Philippine Islands was awarded the Distinguished Alumnus Award of the University of the Philippines College of Medicine. While in the islands he was also instrumental in setting up the Science Foundation of the Philippines.

Lectures for General Practitioners.—A series of seven informal lectures for general practitioners is scheduled to be given under the auspices of the Department of Health of the City of New York on Saturdays, Oct. 18 to Dec. 6 from 10:30 a. m. to noon in the second floor auditorium of the health department building, 125 Worth St., Manhattan. No registration or fee is required, and physicians who attend can be reached by their offices by calling WOrth 2-6900, ext. 252. The schedule of lectures follows:

Oct. 18, Diagnosis and Treatment of Communicable Diseases in General Practice, Harold T. Fuerst.
Oct. 25, Diseases of the Eye, Bernard Kronenberg.
Nov. 1, Some Developments in the Treatment of the Failing Heart, Harry Gold.
Nov. 8, Skin Diseases in General Practice, J. Lowry Miller.
Nov. 15, Diagnostic Procedures in Cancer Detection, Emerson Day.
Nov. 22, Modern Treatment of Diabetes, Henry Dolger.
Dec. 6, Recent Advances in the Diagnosis and Treatment of Chest Diseases, Walsh McDermott.

PENNSYLVANIA

Cancer Meeting.—The annual meeting and training school of the Pennsylvania Division of the American Cancer Society will be held Oct. 17-19 at Pocono Manor Inn, Pocono Manor. Saturday at 9:15 a. m. Dr. S. Milton Dupertuis, Pittsburgh, will give a Kodachrome demonstration of plastic procedures in therapy on patients with neoplasia, and at 10 a. m. Dr. George T. Pack of New York will speak on "Cancer of the Breast." At 1:30 p. m. there will be a symposium on professional education in cancer, with Dr. S. Gordon Castigliano, Philadelphia, as chairman. Collaborators are as follows:

Ruben Snyderman, Pittsburgh, The Practitioner's Needs in Cancer Education.
Ralph D. Bacon, Erie, Division's Functions in Cancer Education.
Brewster S. Miller, New York, National's Functions in Cancer Education.
W. Kenneth Clark, Harrisburg, Health Department's Functions in Cancer Education.

At 3 p. m. Dr. Pack will conduct a panel discussion on "Malignant Tumors of the Skin."

Philadelphia

Faculty Appointments.—Dr. John English Deitrick, formerly associate professor of medicine, Cornell University Medical College, New York, and presently director of study, Survey of Medical Education, Inc., has been appointed Magee professor of medicine, with a seat on the executive faculty of the Jefferson Medical College of Philadelphia.——Dr. Leandro M. Tocantins has been promoted from associate professor of medicine to professor of clinical and experimental medicine, with a seat on the executive faculty of the Jefferson Medical College of Philadelphia.

RHODE ISLAND

Annual Cancer Conference.—The annual Cancer Conference for Physicians will be held under the auspices of the Rhode Island Medical Society, Oct. 15 at the Memorial Hospital, Pawtucket. The program is as follows:

11. a. m., Early Diagnosis of Cancer of the Lung, Richard H. Overholt, Boston.
11:30 a. m., Air Pollution as a Cancerigenic Factor, Wilhelm C. Hueper, Bethesda, Md.
12 noon, Uterine Cancer—Early Diagnosis (Motion Picture).
2 p. m., Why Detection Clinics? Elmer Friedland, Buffalo.
2: 30 p. m., Relation of Benign Lesions of Breast to the Development of Carcinoma, A. Purdy Stout, New York.
3 p. m., Pigmented Moles and Malignant Melanoma, George T. Pack, New York.
3: 30 p. m., Therapy of Malignancy in Childhood, Sidney Farber, Boston.
4 p. m., General Discussion.

TEXAS

Pediatric Meeting.—The Texas Pediatric Society will hold its annual meeting Oct. 17-18 in Dallas. Guest speakers and their subjects will be as follows:

Dorothy H. Andersen, New York, (1) Celiac Disease and Starch Intolerance and (2) Pathology of Premature and Newborn Infants.
Herbert C. Miller, Kansas City, Kan., (1) Pathogenesis and Clinical Features of Pulmonary Hyaline Membranes in Newborn Infants and (2) Use of Tracheotomy, Intermittent Positive Pressure and Heavy Sedation in Treatment of Children with Respiratory Failure Due to Poliomyelitis.
Waldo E. Nelson, Philadelphia, (1) The Pediatrician and Cerebral Palsy and (2) Errors in Antibiotic Therapy.
Gilbert B. Forbes, Dallas, Effect of Age on Disease and Physiological Response.
J. J. Quilligan Jr., Dallas, Infectious Mononucleosis.
Walter R. Hepner, Galveston, Retrolental Fibroplasia.
Joseph A. Stool, Houston, Recent Trends in Immunization.

WEST VIRGINIA

Cancer Meeting.—A postgraduate meeting, sponsored by the West Virginia Academy of General Practice in cooperation with the West Virginia Cancer Society, will be held at the Hotel Morgan in Morgantown, Oct. 19. Dr. George A. Hahn, assistant professor of gynecology and obstetrics, Jefferson Medical College, Philadelphia, will speak on "Cancer of the Cervix," and Dr. Edward F. Lewison, associate professor of surgery, Johns Hopkins University School of Medicine, Baltimore, will discuss "Cancer of the Breast."

WISCONSIN

Conference on Physicians and Schools.—The First Wisconsin Conference on Physicians and Schools will be held in the Memorial Union Building, Madison, Oct. 17-18. The program will include the following presentations:

George Watson, LL.D., Carl N. Neupert, and Mrs. Joseph Born, Our Stake in a Good School Health Program in Wisconsin.
W. W. Bauer, Director, A. M. A. Bureau of Health Education, Chicago. What This Conference Should Accomplish.
Mr. Clyde Parker, Cedar Rapids, Iowa, Let's Really Do a Job.
George M. Wheatley, New York, The Doctor Looks at School Health.
William D. Stovall, Madison, The Early Beginning.

On Friday from 2:15 to 3:30 p. m. and 3:45 to 5:15 p. m. and on Saturday from 9:30 to 11 a. m. there will be workshop discussion group meetings on health examinations, control of disease, emergency care in schools, physical education, athletics and recreation, and emotional problems of the growing child. Fred V. Hein, Ph.D., Consultant in School Health, A. M. A. Bureau of Health Education, Chicago, will give a general evaluation of the conference at the Saturday afternoon session.

GENERAL

Course in Cardiology.—The Albert Einstein Medical Center in cooperation with the American Academy of General Practice is arranging a postgraduate course in cardiology to be given at its northern division, beginning Oct. 15, and continuing for 12 Wednesday sessions (3 to 5:30 p. m.) Registration is limited; the fee is $50. Information may be obtained from Dr. Franklin C. Fetter, Albert Einstein Medical Center, Northern Division, York and Tabor Roads, Philadelphia 41. (Phone: MI 4-0700).

Gulf Coast Clinical Society.—This society will meet in Pensacola, Fla., Oct. 16-17. Speakers will include:

Robert B. Greenblatt, Augusta, Ga., Treatment of Functional Uterine Bleeding.
Charles P. Bailey, Philadelphia, Surgery for Mitral and Coronary Heart Diseases.
Charles W. Mayo, Rochester, Minn., Treatment of Lesions of the Colon.
Louis T. Byars, St. Louis, Treatment of Postirradiation Injuries.
Charles F. Wilkinson, New York, Nonmalignant Lesions of the Pancreas.
Keith S. Grimson, Durham, N. C., Medical and Surgical Treatment of Hypertension.
Harry E. Ungerleider, New York, Insurance Aspects of Heart Disease.
Willard R. Cooke, Galveston, Texas, Rationalism in Regard to Gynecologic Operations.

Conference on Tuberculosis.—The Mississippi Valley Conference on Tuberculosis and the Mississippi Valley Trudeau Society will hold their annual conference at the Jefferson Hotel, St. Louis, Oct. 16-18. On Thursday at 2 p. m. a session on public health will include discussions on "Community Organization for Mass X-Ray," "Follow-up and Evaluation of Mass X-Ray Surveys," "Special Problem Groups," and "Hospital Admissions." On Friday Dr. Leopold Hofstatter, Koch, Mo., will discuss "Emotional Problems of the Chronically Ill," Dr. John H. Skavlem, Cincinnati, "Research Dollars at Work," and Drs. Wilkie L. Howard and Edna M. Jones, Northville, Mich., "Problems of Tuberculosis in Children."

Medical Library Meeting.—The Midwest Regional Group of the Medical Library Association will meet at the Lilly Research Laboratories, Indianapolis, Oct. 17-18. On Friday at 3:45 p. m. Lieut. Col. Frank B. Rogers will discuss "Armed Forces Medical Library Bibliographic Projects." At 5:15 p. m. there will be a tour of the library business service, followed by dinner at 5:30 in the Lilly private dining room. Saturday at 9:40 a. m. Jeanne Reilley, American Medical Association Library, Chicago, will speak on "What Remains To Be Done in Recruitment at the Local Level," and Virginia Donley, Mercy Hospital, Springfield, Ohio, on "The Medical Librarian and the Medical Record Librarian."

Course in Diabetes.—The first formal postgraduate course ever conducted independently by the American Diabetes Association is to be given Jan. 19-21, 1953, at Toronto, Canada. Dr. Charles H. Best, director of the Banting and Best department of medical research and the department of physiology, University of Toronto, will be director of the course. Dr. Ray F. Farquharson, professor of medicine, will be clinical director, and Dr. Andrew L. Chute, professor of pediatrics, associate clinical director. The course is open to physicians interested in advanced study of clinical medicine and basic medical sciences related to diabetes. Details can be secured from the American Diabetes Association, Inc., 11 W. 42nd St., New York 36.

Meeting of Clinical Pathologists.—The American Society of Clinical Pathologists will hold its 31st annual meeting and 18th seminar at the Drake Hotel, Chicago, Oct. 14-17. Tuesday will be devoted to a joint meeting with the College of American Pathologists, including an all day symposium on fluid and electrolyte balance beginning at 9 a. m. and the annual banquet at 7 p. m. preceded by a reception (*J. A. M. A.* **150:**499 [Oct. 4] 1952). At the banquet the Ward Burdick award will be presented to Dr. Alfred S. Giordano, South Bend, Ind., and a scroll of merit to Dr. Arthur H. Sanford, Rochester, Minn. On Friday from 9 to 5 p. m., in the Grand Ballroom, a seminar on "Some Obstetric and Gynecologic Neoplasms" will be conducted by Dr. Arthur T. Hertig, Shattuck professor of pathological anatomy at Harvard Medical School, Boston. Dr. Lauren V. Ackerman, St. Louis, will serve as moderator. The seminar is limited to registrants.

American Dietetic Association Meeting in Minneapolis.—The American Dietetic Association will hold its annual meeting Oct. 21-24 in Minneapolis. About 3,500 dietitians, nutritionists, and guests, including scientists and members of the medical profession who are working in related fields, are expected to attend. Invited speakers will include:

Olaf Mickelsen, Ph.D., Bethesda, Md., Newer Findings in Nutrition Research.
Nathaniel E. Rossett, Memphis, Dietetic Management of Peptic Ulceration.
Sumner S. Cohen, Oak Terrace, Minn., Trends in Nutrition for Patients with Pulmonary Tuberculosis.
Clifford F. Gastineau, Rochester, Minn., Stress and Nutrition.
Rachmiel Levine, Chicago, Dietary Therapy of Gout.
Priscilla White, Boston, Newer Findings in Renalvascular Diseases.

Ancel B. Keys, Ph.D., director of the laboratory of physiological hygiene at the University of Minnesota, Minneapolis, will speak on "Diet and Health Problems of the Western World." Speaking at the Thursday noon luncheon, Dr. Walter R. Ramsey, medical director, Children's Hospital, St. Paul, will explain "Some of the Problems Met During 50 Years in Child Nutrition." A panel discussion on obesity has been planned, in which Dr. Frederick J. Stare, head of the department of nutrition, School of Public Health, Harvard University, will describe studies on weight reduction conducted by his department; Dr. Daniel A. Glomset of Des Moines, will talk on the "Philosophy of Adiposity," and Ruth M. Leverton, Ph.D., of the University of Nebraska and author of the recent book "Food Becomes You," will give a "Comparison of Low-Calorie Diets." Other speakers are to be Dr. Grace A. Goldsmith, professor of medicine, Tulane University, New Orleans, and Dr. Jonathan E. Rhoads, professor of surgery, University of Pennsylvania, Philadelphia, both of the National Research Council, who will present "A Consideration of the Supranormal Dietary Requirements of Certain Acutely Ill Patients."

Life Insurance Medical Meeting.—The Association of Life Insurance Medical Directors of America will hold its annual meeting Oct. 21-23 at the Ambassador Hotel, Los Angeles. Tuesday, 10 a. m., an address of welcome will be delivered by Dr. Lewis A. Alesen, Los Angeles, president, California State Medical Association. Other speakers Tuesday morning will be Dr. George C. Griffith, Los Angeles, on "Problems in Borderline Cardiovascular Disease States," and Dr. John W. Gofman, Berkeley, on "Present Status of Lipid Metabolic Disturbances and Their Relation to the Genesis of Arterial Disease." After luncheon, Dr. Myron Prinzmetal, Los Angeles, will present "Irregularities of the Heart Beat."

The annual reception and banquet will be held at 6:30 p. m. Wednesday. Dr. Stafford L. Warren, dean, School of Medicine, University of California at Los Angeles, and director of the university's atomic energy project, will speak on "Living in the Atomic Age." Other speakers during the sessions include:

Francis A. L. Mathewson, Winnipeg, Manitoba, Prolonged P-R Interval in Apparently Healthy People.
Ralph M. Filson, Hartford, Conn., The Business of Insurance and the Profession of Medicine.
Robert H. Williams, Seattle, Syncope, Vertigo, Dizziness.
Alan R. Moritz, Cleveland, Trauma and Heart Disease.
Charles W. Barnett, Los Angeles, Prognosis in Latent Syphilis.
William A. Winn, Springville, Calif., Coccidioidomycosis.
John B. Doyle, Los Angeles, Diseases of the Muscles and Neuromuscular Junctions.
John W. Wear, San Francisco, Observations of a Medical Referee.

Pediatric Meeting in Chicago.—The American Academy of Pediatrics will hold its annual meeting at the Palmer House, Chicago, Oct. 18-23. A seminar on Saturday (repeated Sunday) will be devoted to pediatric neurology, metabolic diseases, pediatric allergy, emotional problems in children, pediatric cardiology, virus and rickettsial diseases, hematology, endocrinology, and disturbances of acid base and water metabolism. The section meeting on mental growth and development, Sunday, 8 p. m., open to all members, will include presentations on "Personality Development in Infancy and Childhood," "Problems Arising Around Normal Development," and "Emotional Management of the Hospitalized Child." Monday morning there will be a symposium on hydrazine derivatives of isonicotinic acid and Monday afternoon a symposium on surgical problems in childhood. Monday evening at 8 p. m. the American Academy of Pediatrics and the National Safety Council will hold a joint meeting. A progress report of a pilot study of childhood accidents will be presented by Dr. William Langford, New York, and pathological studies concerning the nature of "mechanical suffocation" in the young, by Dr. Sidney Farber, Boston. The session will end with a dramatization on "Community Action for Child Accident Prevention." Monday (2 to 5 p. m.) and Tuesday (9 a. m. to noon) there will be round-table discussions on psychological disturbances during adolescence, pediatric endocrinology, the adolescent girl and her menstrual problems, clinical pediatric urology, problems of the premature and newborn, hearing and speech difficulties in children, pediatric x-ray examinations, accident prevention in children, encephalography and pneumoencephalography, antibiotics, and management of poliomyelitis including bulbar and respiratory involvement. Tuesday morning there will be a symposium on the effect of abnormal states on renal physiology and Tuesday afternoon a symposium on hearing, speech, and reading difficulties in children. The Tuesday evening session will be held at the Museum of Science and Industry at 8 p. m., when a panel discussion will be presented on "Audiovisual Aids to Education." Tuesday (2 to 5 p. m.) and Wednesday (9 a. m. to noon) the following round-table discussions will be held: use of corticotropin, cortisone, and associated substances; rheumatic fever; problems in child psychiatry; emergency care of the newborn; celiac syndrome; evaluation of mental deficiencies; pediatric dermatology; pediatric allergy; blood dyscrasias; pediatric pathology; and nature, recognition, and management of neuromuscular disabilities in children. On Wednesday morning there will be a symposium on neurological conditions in children and the presentation of scientific award papers. Thursday morning a symposium will be presented on basic mechanisms in allergic diseases. Thursday afternoon clinical conferences will be held at Children's Memorial Hospital; children's division, Cook County Hospital; Bobs Roberts Memorial Hospital for Children; and Sarah Morris Hospital for Children, Michael Reese Hospital.

Annual Public Health Meeting.—The 80th annual meeting of the American Public Health Association and the annual meetings of the 38 related organizations will be held in the public auditorium, Cleveland, Oct. 20-24. On Monday at 9:30 a. m. a panel discussion will be presented on "The Relationship of State Public Health Laboratories to the Private and Hospital Laboratories" and at 2:30 one on "Pictographic Versus Manual Reproduction of Laboratory Reports and Records."

Tuesday at 9:30 a. m. the maternal and child health section and the American School Health Association will conduct a joint session for the discussion of developments in programs for crippled children. The statistics section, the American Association of Registration Executives, and the American Association of Medical Record Librarians will hold a joint session to discuss the role of the medical record librarians in public health statistics. At the first general session, at 8:30 p. m., Dr. Gaylord W. Anderson, Minneapolis, will deliver the presidential address on "The Scope of Public Health." Addresses of welcome will be made by the Hon. Frank J. Lausche, governor of Ohio, the Hon. Thomas A. Burke, mayor of Cleveland, and Dr. Harold J. Knapp, commissioner of health, Cleveland. The Lasker awards for 1952 will be presented. On Wednesday at 2:30 p. m. the first special session will be held to consider the subject "Measuring Public Health." Dr. John D. Porterfield, Columbus, Ohio, will present "Problems and Definitions" and will participate in a panel discussion of program evaluation with Drs. Charles E. Reddick, Louisville, Charles F. Sutton, Springfield, Ill., and Jesse B. Spielholz, Seattle. At 6 p. m. the American School Health Association will celebrate its 25th anniversary with a dinner session in the Assembly Room of the Hollenden Hotel. Dr. Howard A. Rusk, New York, will speak on "Crippled Children in a Crippled World." Thursday at 2:30 p. m. hepatitis and leptospirosis will be discussed at a joint session of the epidemiology and laboratory sections. The food and nutrition section will hold a panel discussion "Obesity—America's No. 1 Health Problem," with Dr. Norman Jolliffe, New York, as moderator. Dr. Leonard A. Scheele, will preside at the Joseph W. Mountin memorial session on "Advancing the Frontiers of Public Health," which will be presented at the joint session of health officers, industrial hygiene, medical care, and public health nursing sections. School health policies will be considered at the joint session of health officers, maternal and child health,

public health education, public health nursing, and school health sections, and the American School Health Association. At 7 p. m. the second general session will convene at the annual banquet, which will be held in the Grand Ballroom of the Statler Hotel. Dr. Brock Chisholm, director-general, World Health Organization, Geneva, Switzerland, will speak on "Human Relations in World Health." "The Control of Tuberculosis in 1952" is the subject of the second special session, which will be held Friday at 2:30 p. m.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories, and possessions in the weeks ended as indicated:

Area	Sept. 20, 1952	Sept. 13, 1952	Sept. 22, 1951
New England States			
Maine	9	9	2
New Hampshire	4	4	4
Vermont	3	5	2
Massachusetts	35	44	9
Rhode Island	9	8	1
Connecticut	27	35	14
Middle Atlantic States			
New York	177	189	121
New Jersey	58	55	41
Pennsylvania	152	107	64
East North Central States			
Ohio	283	264	89
Indiana	152	107	31
Illinois	436	352	116
Michigan	260	274	99
Wisconsin	223	166	151
West North Central States			
Minnesota	388	405	41
Iowa	202	276	34
Missouri	85	91	55
North Dakota	21	12	5
South Dakota	87	57	7
Nebraska	209	212	38
Kansas	180	181	58
South Atlantic States			
Delaware	7	8	..
Maryland	19	11	4
District of Columbia	8	9	1
Virginia	47	37	20
West Virginia	42	49	9
North Carolina	27	36	11
South Carolina	13	12	4
Georgia	29	23	24
Florida	30	29	4
East South Central States			
Kentucky	151	162	12
Tennessee	44	43	59
Alabama	18	19	24
Mississippi	39	28	59
West South Central States			
Arkansas	19	28	24
Louisiana	33	41	47
Oklahoma	87	61	33
Texas	117	151	73
Mountain States			
Montana	15	21	28
Idaho	16	34	6
Wyoming	10	8	9
Colorado	53	45	41
New Mexico	25	30	8
Arizona	16	13	14
Utah	15	16	26
Nevada	..	3	5
Pacific States			
Washington	88	80	30
Oregon	27	24	17
California	196	189	172
Territories and Possessions			
Alaska	..	..	5
Hawaii	2	2	..
Puerto Rico	..	2	..
Total	4,193	4,067	1,751

CORRECTION

Course in Ophthalmology at Yale.—The first three presentations in the 1953 postgraduate courses in ophthalmology, Yale University School of Medicine, New Haven, Conn., will be as follows and not as given in THE JOURNAL, Sept. 27, on page 422:

Jan. 9, Case Presentations, Francis P. Guida, New Haven.
Jan. 30, Round-Table Discussion of Surgical Problems and Their Management, Edmund B. Spaeth, Philadelphia.
Feb. 13, Case Presentations, Clement C. Clarke, New Haven.

Dr. Musella's Book Review.—The review of the book "Il cancro," published in THE JOURNAL, Aug. 23, 1952, page 1608, incorrectly stated that the author is a layman. Mario Musella, author of this book, is a doctor of medicine and has for many years been active in university clinics and hospitals in Italy.

MEETINGS

AMERICAN MEDICAL ASSOCIATION CLINICAL SESSION, Denver, Dec. 2-5. Dr. George F. Lull, 535 North Dearborn Street, Chicago 10, Secretary.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, Chicago, Oct. 12-17. Dr. W. L. Benedict, 100 First Avenue Bldg., Rochester, Minn., Executive Secretary.

AMERICAN ACADEMY OF DERMATOLOGY AND SYPHILOLOGY, Palmer House, Chicago, Dec. 6-11. Dr. John E. Rauschkolb, P.O. Box 6565, Cleveland 1, Secretary.

AMERICAN ACADEMY OF PEDIATRICS, Palmer House, Chicago, Oct 20-23. Dr. E. H. Christopherson, 610 Church St., Evanston, Ill., Secretary.

AMERICAN ACADEMY OF TROPICAL MEDICINE, Galveston, Texas, Nov. 13-15. Dr. Clay G. Huff, Navy Medical Research Institute, Bethesda 14, Md., Secretary.

AMERICAN ASSOCIATION OF MEDICAL CLINICS, Cosmopolitan Hotel, Denver, Nov. 30-Dec. 1. Dr. Edwin P. Jordan, Box 114, Charlottesville, Va., Executive Director.

AMERICAN ASSOCIATION OF MEDICAL RECORD LIBRARIANS, Shoreham Hotel, Washington, D. C., Oct. 13-17. Miss Doris Gleason, 510 N. Dearborn St., Chicago 10, Executive Secretary.

AMERICAN CANCER SOCIETY, Park Sheraton Hotel, New York, Oct. 21-22. Dr. Brewster S. Miller, 47 Beaver St., New York 4, Director.

AMERICAN CLINICAL AND CLIMATOLOGICAL ASSOCIATION, Elmira, N. Y., Oct. 16-18. Dr. Marshall N. Fulton, 124 Waterman St., Providence 6, R. I., Secretary.

AMERICAN DIETETIC ASSOCIATION, Minneapolis Auditorium, Minneapolis, Oct. 21-24. Miss Ruth M. Yakel, 620 North Michigan Avenue, Chicago 11, Executive Secretary.

AMERICAN PSYCHOANALYTIC ASSOCIATION, New Yorker Hotel, New York, Dec. 4-7. Dr. LeRoy M. A. Maeder, 1910 Rittenhouse Square, Philadelphia 3, Secretary.

AMERICAN PUBLIC HEALTH ASSOCIATION, Public Auditorium, Cleveland, Oct. 20-24. Dr. Reginald M. Atwater, 1790 Broadway, New York 19, Executive Secretary.

AMERICAN SOCIETY OF ANESTHESIOLOGISTS, Philadelphia, Nov. 11-14. Dr. J. Earl Remlinger Jr., Suite 1101, 188 West Randolph Street, Chicago 1, Secretary.

AMERICAN SOCIETY OF CLINICAL PATHOLOGISTS, Chicago, Oct. 13-17. Dr. Clyde G. Culbertson, 1040 W. Michigan St., Indianapolis, Secretary.

AMERICAN SOCIETY FOR THE STUDY OF ARTERIOSCLEROSIS, Hotel Knickerbocker, Chicago, Nov. 9-10. Dr. O. J. Pollak, P. O. Box 228, Dover, Del., Secretary.

AMERICAN SOCIETY OF TROPICAL MEDICINE AND HYGIENE, Galvez Hotel, Galveston, Texas, Nov. 13-15. Dr. Quentin M. Geiman, 25 Shattuck St., Boston 15, Secretary.

ASSOCIATION OF AMERICAN MEDICAL COLLEGES, The Broadmoor, Colorado Springs, Colo., Nov. 10-12. Dr. Dean F. Smiley, 185 North Wabash Ave., Chicago 1, Secretary.

ASSOCIATION OF LIFE INSURANCE MEDICAL DIRECTORS OF AMERICA, Los Angeles, Oct. 21-23. Dr. Henry B. Kirkland, P. O. Box 594, Newark 1, N. J., Secretary.

ASSOCIATION OF MILITARY SURGEONS OF THE UNITED STATES, Hotel Statler, Washington, D. C., Nov. 17-19. Dr. R. R. Sayers, Armed Forces Institute of Pathology, Washington 25, D. C., Secretary.

COLLEGE OF AMERICAN PATHOLOGISTS, Drake Hotel, Chicago, Oct. 13-17. Dr. M. G. Westmoreland, 203 N. Wabash Ave., Chicago 1, Executive Secretary.

CONGRESS OF NEUROLOGICAL SURGEONS, Palmer House, Chicago, Nov. 6-7. Dr. Bland W. Cannon, 1092 Madison Ave., Memphis, Tenn., Secretary.

GREAT FALLS MEDICAL-SURGICAL CONFERENCE, Great Falls, Mont., Oct. 24-25. Dr. William E. Sullens, Box 1066, Great Falls, Mont., Chairman.

GULF COAST CLINICAL SOCIETY, San Carlos Hotel, Pensacola, Fla., Oct. 16-17. Dr. Dale E. York, 21½ E. Wright St., Pensacola, Fla., Secretary.

INDIANA STATE MEDICAL ASSOCIATION, Murat Temple, Indianapolis, Oct. 28-30. Mr. James A. Waggener, 23 E. Ohio St., Indianapolis 4, Executive Secretary.

INTERSTATE POST GRADUATE MEDICAL ASSOCIATION OF NORTH AMERICA, Public Auditorium, Cleveland, Nov. 10-13. Dr. Arthur G. Sullivan, 16 North Carroll St., Madison, Wis., Managing Director.

NATIONAL ASSOCIATION FOR MENTAL HEALTH, Henry Hudson Hotel, New York, Nov. 17-19. Dr. George S. Stevenson, 1790 Broadway, New York, Medical Director.

NATIONAL GASTROENTEROLOGICAL ASSOCIATION, Hotel Statler, New York, Oct. 20-22. Dr. A. Xerxes Rossien, 1819 Broadway, New York 23, Secretary.

NEW ENGLAND OBSTETRICAL AND GYNECOLOGICAL SOCIETY, Hotel Somerset, Boston, Oct. 29. Dr. Carmi R. Alden, 270 Commonwealth Ave., Boston 16, Secretary.

NEW ENGLAND POSTGRADUATE ASSEMBLY, Hotel Statler, Boston, Oct. 28-30. Dr. Laurence B. Ellis, 22 Fenway, Boston, Chairman.

NORTH PACIFIC SURGICAL ASSOCIATION, Spokane, Wash., Nov. 21-22. Dr. John A. Duncan, 509 Olive Way, Seattle, Secretary.

OKLAHOMA CITY CLINICAL SOCIETY, Biltmore Hotel, Oklahoma City, Oct. 27-30. Dr. N. L. Miller, 512 Medical Arts Bldg., Oklahoma City, Director of Clinics.

OMAHA MID-WEST CLINICAL SOCIETY, Hotel Paxton, Omaha, Oct. 27-31. Dr. Payson S. Adams, 1031 Medical Arts Bldg., Omaha 2, Director of Clinics.

POSTGRADUATE ASSEMBLY IN ENDOCRINOLOGY AND METABOLISM, Roney Plaza Hotel, Miami Beach, Fla., Nov. 3-8. Dr. Henry H. Turner, 1200 N. Walker Street, Oklahoma City 3, Okla., Secretary.

SAN ANTONIO TUMOR SEMINAR, Annex 4, Brooke Army Hospital, San Antonio, Texas, Nov. 1. Dr. A. O. Severance, 205 Camden St., San Antonio 2, Texas, Secretary.

SOUTHERN ELECTROENCEPHALOGRAPHIC SOCIETY, Sorrento Hotel, Miami Beach, Fla., Nov. 10-11. Dr. Irving Pine, Columbus Receiving Hospital, Columbus, Ohio, Secretary.

SOUTHERN MEDICAL ASSOCIATION, Miami, Fla., Nov. 10-13. Mr. C. P. Loranz, 1020 Empire Bldg., Birmingham 3, Ala., Secretary.

SOUTHERN PSYCHIATRIC ASSOCIATION, White Sulphur Springs, W. Va., Nov. 2-5. Dr. N. M. Owensby, Medical Arts Bldg., Atlanta 3, Ga., Secretary.

SOUTHWESTERN MEDICAL ASSOCIATION, Hilton Hotel, Albuquerque, N. M., Oct. 30-Nov. 1. Dr. W. W. Schuessler, 1415 First National Bank Bldg., El Paso, Texas, Secretary.

SOUTHWESTERN SURGICAL CONGRESS, Baker Hotel, Dallas, Texas, Oct. 20-22. Miss June Marchant, 1227 Classen St., Oklahoma City, Executive Secretary.

WESTERN SURGICAL ASSOCIATION, The Shamrock, Houston, Texas, Dec. 4-6. Dr. Michael L. Mason, 154 East Erie St., Chicago 11, Secretary.

INTERNATIONAL

CONGRESS OF INTERNATIONAL LEAGUE AGAINST RHEUMATISM, Geneva and Zurich, Switzerland, Aug. 24-29. For information write: Dr. W. Tegner, The London Hospital, London E.1, England.

CONGRESS OF THE INTERNATIONAL SOCIETY OF SURGERY, Lisbon, Portugal, Sept. 15-20, 1953. Dr. L. Dejardin, 141, rue Belliard, Brussels, Belgium, General Secretary.

INTER-AMERICAN CONGRESS OF RADIOLOGY, Mexico City, Mexico, Nov. 2-8. Dr. Guido Torres Martinez, Marsella No. 11, Mexico, D.F., Secretary-General.

INTER-AMERICAN SESSION, American College of Surgeons, Paulista Medical Association Bldg., Sao Paulo, Brazil, Feb. 9-12, 1953. Dr. Moacyr Eyck Alvaro, 1151 Conselacao, Sao Paulo, Brazil, Chairman.

INTERNATIONAL CONGRESS OF ELECTROENCEPHALOGRAPHY AND CLINICAL NEUROPHYSIOLOGY, Boston, Mass., U. S. A., Aug. 18-21, 1953. Dr. Robert S. Schwab, Massachusetts General Hospital, Boston 14, Mass., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS FOR HISTORY OF SCIENCE, Jerusalem, Israel, August 3-7, 1953. Prof. F. S. Bodenheimer, Hebrew University, Jerusalem, Israel, President.

INTERNATIONAL CONGRESS ON HYDATID DISEASE, Santiago, Chile, Nov. 21-24. Organizing Committee, P. O. Box 9183, Santiago, Chile.

INTERNATIONAL CONGRESS ON MEDICAL LIBRARIANSHIP, London, England, July 20-25, 1953. Mr. W. R. LeFanu, % London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1, England, Chairman.

INTERNATIONAL CONGRESS OF MICROBIOLOGY, Rome, Italy, Sept. 6-12, 1953. For information write: Dr. V. Puntoni, Citta Universitaria, Rome, Italy.

INTERNATIONAL CONGRESS OF MILITARY MEDICINE AND PHARMACY, Montevideo, Uruguay, March 1-7, 1953. Dirreccion General del Servico de Sanitad Militar, 8 de Octubre y Mariano Moreno, Montevideo, Uruguay, Secretariat of the Congress.

INTERNATIONAL CONGRESS OF OTORHINOLARYNGOLOGY, Amsterdam, Netherlands, June 8-15, 1953. Dr. W. H. Struben, J. J. Viottastraat 1, Amsterdam, Netherlands, Secretary.

INTERNATIONAL CONGRESS OF RADIOLOGY, Copenhagen, Denmark, July 19-25, 1953. Professor Flemming Norgaard, 10 Oster Voldgade, Copenhagen K., Denmark, Secretary General.

INTERNATIONAL CONGRESS OF THERAPEUTICS, Madrid, Spain, Oct. 16-18. Professor Armijo, Instituto de Farmacologia, Cuidad Universitaria, Madrid, Spain, Secretary.

INTERNATIONAL CONGRESSES OF TROPICAL MEDICINE AND MALARIA, Istanbul, Turkey, Aug. 28-Sept. 4, 1953. Professor Dr. Ihsan Sükrü Aksel, Tunel Meydam, Beyoglu, Istanbul, Turkey, General Secretary.

INTERNATIONAL HOSPITAL CONGRESS, London, England, May 25-30, 1953. Capt. J. E. Stone, 10 Old Jewry, London, EC2, England, Hon. Secretary.

INTERNATIONAL PHYSIOLOGICAL CONGRESS, Montreal, Canada, Aug. 31-Sept. 4, 1953. Dr. A. S. V. Burgen, Dept. of Physiology, McGill University, Montreal, Canada, Secretary.

INTERNATIONAL STUDY CONFERENCE ON CHILD WELFARE, Bombay, India, Dec. 5-12. For information write: All India Save the Children Committee, 5 Carmichael Road, Bombay, India.

PAN AMERICAN CONGRESS OF THE MEDICAL PRESS, Buenos Aires, Argentine, July 12-16, 1953. Secretaria del Congress, 763 Uriburu, Buenos Aires, Argentine.

WORLD CONFERENCE ON MEDICAL EDUCATION, British Medical Association House, Tavistock Square, W.C.1, London, England, Aug. 24-29, 1953. Secretariat: World Medical Association, 2 East 103d St., New York 29, N. Y., U. S. A.

WORLD CONGRESS OF MEDICINE, Montecatini, Italy, Oct. 16-18. Secretariat: Corso Trieste, 65, Rome, Italy.

WORLD CONGRESS OF THE WORLD CONFEDERATION FOR PHYSICIAL THERAPY, London, England, Sept. 7-12, 1953. Miss M. J. Neilson, Chartered Society of Physiotherapy, Tavistock House, South, Tavistock Square, London, W.C.1, England, Secretary.

WORLD MEDICAL ASSOCIATION, Athens, Greece, Oct. 12-16. Dr. Louis H. Bauer, 2 East 103d St., New York 29, N. Y., Secretary General.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Part I and II.* February 1953. All centers where there are five or more candidates. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia 4.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* Various locations, July 17. Final date for filing applications is January 17. Sec., Dr. C. B. Hickcox, 80 Seymour St., Hartford 15.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Oral.* Philadelphia, October 1953. Final date for filing application is May 1. Ex. Sec., Miss Janet Newkirk, 66 East 66th St., New York 21.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Various centers and overseas, Oct. 20. Closing date for the acceptance of applications for the written examination was May 1. *Oral.* Philadelphia, Nov. 13-14 and Washington, D. C., Nov. 17-18. Exec. Sec.-Treas., Dr. William A. Werrell, 1 West Main Street, Madison 3.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* Chicago, May or June 1953. Final date for filing application for the oral examination is Jan. 15, 1953. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, Kingshighway and Euclid Ave., St. Louis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written.* Various Centers, Feb. 6, 1953. Final date for filing applications is Nov. 1. Sec., Dr. R. L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Written.* Various Centers, January 1953. Final date for filing applications was July 1. *Practical.* New York City, June 6-10, 1953. Sec., Dr. Edwin B. Dunphy, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: The deadline for the receipt of applications for the 1953 Part II examinations was Aug. 15; for the 1953 Part I examination the deadline is Nov. 30. Sec., Dr. Harold A. Sofield, 122 S. Michigan Ave., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Written.* Chicago, Oct. 6-10. *Oral.* Chicago, Oct. 6-10 and New Orleans, April 21-25, 1953. Sec., Dr. Dean M. Lierle, University Hospital, Iowa City.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Chicago, Oct. 24-26; Boston, Dec. 5-7. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION. *Oral and Written.* June 1953. Final date for filing applications is March 15. Sec., Dr. Robert L. Bennett, 30 N. Michigan Blvd., Chicago.

AMERICAN BOARD OF PREVENTIVE MEDICINE AND PUBLIC HEALTH: Cleveland, Oct. 18-20. Sec., Dr. E. L. Stebbins, 615 N. Wolfe St., Baltimore.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York City, Dec. 15-16. Final date for filing applications was Sept. 15. Sec.-Treas., Dr. David A. Boyd, Jr., 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Oral.* Dec. 1-7. Final date for filing application was June 1. *Oral.* Tampa, April 8-15. Sec., Dr. B. R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written.* Various Centers, March 1953. Final date for filing application is Dec. 1. Sec., Dr. John B. Flick, 225 S. 15th St., Philadelphia.

AMERICAN BOARD OF UROLOGY: *Written.* Various Centers, December. *Oral.* Chicago, Feb. 7-11. Sec., Dr. Harry Culver, 30 Westwood Road, Minneapolis 16, Minn.

DEATHS

Smith, Earle Terry ⊕ West Hartford, Conn.; born in Bridgeport, Conn., Sept. 2, 1876; Yale University School of Medicine, New Haven, 1897; specialist certified by the American Board of Ophthalmology; past president of the Connecticut State Medical Society; member of the American Academy of Ophthalmology and Otolaryngology, American Laryngological, Rhinological and Otological Society, American Ophthalmological Society, American Otological Society, and the Association for Research in Ophthalmology; fellow of the American College of Surgeons; served in France during World War I; affiliated with J. J. McCook Memorial Hospital, Institute of Living, St. Francis Hospital, New Britain (Conn.) General Hospital, Manchester (Conn.) Memorial Hospital, Johnson Memorial Hospital in Stafford Springs, Bristol (Conn.) Hospital, and Hartford Hospital, of which he was a member of the board of directors; received an honorary degree of master of arts from Trinity College, Hartford, in 1903; died July 23, aged 75, of carcinoma of the esophagus.

McDonald, James Francis ⊕ New York City; born Nov. 22, 1881; Syracuse University College of Medicine, 1911; specialist certified by the American Board of Psychiatry and Neurology; assistant in anatomy at Bellevue Hospital Medical College, 1911-1912; professor of anatomy at Fordham University School of Medicine from 1912 to 1918; formerly fellow in surgery at Mayo Foundation in Rochester, Minn.; professor of physiology at Creighton University School of Medicine in Omaha from 1921 to 1930; assistant professor of neuroanatomy from 1935 to 1937 at New York Post Graduate Medical School and Hospital, Columbia University, where from 1937 to 1948 he was assistant professor of clinical neurology and psychiatry; affiliated with St. Joseph's Hospital in Yonkers, N. Y., Fordham Hospital, St. Clare's Hospital, St. Elizabeth's Hospital, and St. Vincent's Hospital, where he died Aug. 15, aged 70, of cancer.

Strome, Frank Paul ⊕ Colonel, U. S. Army, retired, Drexel Hill, Pa.; born in Ashley, Pa., April 15, 1887; Medico-Chirurgical College of Philadelphia, 1915; commissioned in the medical corps of the U. S. Army in June, 1917; served overseas during World War I; retired from active duty in 1934; recalled to active service in August, 1940; served as deputy surgeon and surgeon for the Third Service Command from August, 1942, to October, 1945; retired in 1946, when he was awarded the Legion of Merit for maintaining exceptionally high standards of health throughout the command; fellow of the American College of Physicians; formerly professor of military science and tactics at Jefferson Medical College; at one time director of the bureau of vital statistics, state board of health, at Harrisburg; died July 28, aged 65.

Ahearne, Cornelius Augustus Jr. ⊕ Marblehead, Mass.; Harvard Medical School, Boston, 1889; formerly practiced in Salem, where he was city physician; died at Mary A. Alley Emergency Hospital July 21, aged 84, of heart disease.

Archer, Palmer Marion, Houston, Texas; University of Pennsylvania Department of Medicine, Philadelphia, 1910; emeritus professor of clinical otolaryngology at Baylor University College of Medicine; specialist certified by the American Board of Otolaryngology; fellow of the American College of Surgeons; on the courtesy staffs of St. Joseph's Infirmary, Memorial Hospital, and Methodist Hospital; consultant in otolaryngology at Hermann Hospital, where he died July 3, aged 67, of a heart attack.

Blaine, Mitchell ⊕ Mammoth Spring, Ark.; Kansas City (Mo.) College of Medicine and Surgery, 1926; St. Louis College of Physicians and Surgeons, 1923; died May 23, aged 56.

Carson, William George, Los Angeles; College of Physicians and Surgeons, Los Angeles, 1917; died July 28, aged 69, of bronchopneumonia and encephalitis.

Coats, Jasper M., Cabool, Mo.; American Medical College, St. Louis, 1899; died April 26, aged 83, of heart disease.

Conlon, Leo Vincent ⊕ Woonsocket, R. I.; Tufts College Medical School, Boston, 1921; past president of the Woonsocket District Medical Society; served during World War I; affiliated with Woonsocket Hospital; died in Phillips House, Massachusetts General Hospital in Boston, July 18, aged 55, of congestive heart failure and pulmonary embolus.

Dolan, William Edward ⊕ Worcester, Mass.; Baltimore Medical College, 1902; member of the New England Ophthalmological Society and New England Otolaryngological Society; affiliated with St. Vincent Hospital, where he died July 21, aged 73, of coronary thrombosis.

Ferguson, Clara ⊕ Gibson Island, Md.; Northwestern University Woman's Medical School, Chicago, 1894; member of the Illinois State Medical Society; an Associate Fellow of the American Medical Association; died June 21.

Ferrell, Jesse Egbert ⊕ Fortville, Ind.; Medical College of Indiana, Indianapolis, 1903; past president of the Indiana State Medical Association; affiliated with Methodist Hospital in Indianapolis and St. John's Hospital in Anderson, where he died July 2, aged 71, of cerebral hemorrhage and hypertension.

Ferris, Francis Scoffin, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1895; formerly chief medical officer for the Reading Terminal; served during World War I; later commissioned a lieutenant colonel in the medical reserve corps; at one time deputy of the state board of health and medical consultant for the municipal court; died in Abington (Pa.) Memorial Hospital July 28, aged 80, of arteriosclerotic heart disease and heart block.

Foreman, Arthur Petherick ⊕ Syracuse, N. Y.; Syracuse University College of Medicine, 1916; clinical associate professor emeritus of pediatrics at his alma mater; specialist certified by the American Board of Pediatrics; affiliated with Syracuse Memorial Hospital; died July 7, aged 72.

Foster, Paul Cameron ⊕ Gallipolis, Ohio; University of Chicago, The School of Medicine, 1937; fellow of the American College of Surgeons; affiliated with Holzer Hospital, where he died July 26, aged 49, of intracerebral hemorrhage.

Fulton, George ⊕ Oklahoma City, Okla.; Memphis (Tenn.) Hospital Medical College, 1904; died in St. Anthony Hospital July 1, aged 71, of carcinoma of the prostate and liver.

Garrett, Robert C., Eagleville, Tenn.; University of Tennessee College of Medicine, Memphis, 1900; affiliated with Rutherford Hospital in Murfreesboro; died July 2, aged 79, of a heart attack.

Garrison, Clinton Dudley, Daytona Beach, Fla.; Miami Medical College, Cincinnati, 1903; died in South Daytona Beach recently, aged 75, of pulmonary embolism and thrombophlebitis.

Goldberg, Sidney Isaac, New York; University and Bellevue Hospital Medical College, New York, 1921; member of the American Trudeau Society; died July 13, aged 54.

Gray, John Wilson ⊕ Geneva, Ill.; University of Illinois College of Medicine, Chicago, 1930; member of the school board; served during World War II; on the staff of the Community Hospital, where he died recently, aged 51, of coronary thrombosis.

Hammer, Walter Paul, Falls Church, Va.; Chicago College of Medicine and Surgery, 1916; past president of the Arlington County Medical Society; member of the Selective Service System during World War II; recipient of the Congress Selective Service Medal and four Selective Service certificates from the President of the United States; affiliated with Garfield, Georgetown University, and Doctors hospitals in Washington, D. C., Alexander (Va.) Hospital, and Arlington Hospital, where he died July 14, aged 62, of postoperative infection.

⊕ Indicates Member of the American Medical Association.

Holm, Peter Frederick ✠ Sarasota, Fla.; Bellevue Hospital Medical College, New York, 1898; member of the Minnesota State Medical Association; while practicing in Wells, Minn., he was president of the Faribault County Medical Society, physician for the board of health, and for many years coroner; died June 11, aged 79, of congestive heart failure.

Lynch, George Hubert, Big Rapids, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1903; served as mayor; affiliated with Community Hospital, where he died June 5, aged 73, of cerebral hemorrhage.

McCormick, George Warren, Zanesville, Ohio; Medical College of Ohio, Cincinnati, 1897; died May 12, aged 78, of arteriosclerosis.

Parker, Frank Claveloux ✠ Norristown, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1899; fellow of the American College of Surgeons; consulting surgeon, Wills Hospital, Philadelphia; consulting ophthalmologist, Memorial Hospital in Philadelphia, Norristown State Hospital, and the Montgomery Hospital, where he died July 2, aged 74, of angina pectoris.

Piercy, Robert Lee, Youngstown, Ohio; University of Rochester School of Medicine and Dentistry, 1938; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; served during World War II; died in North Side Hospital July 2, aged 39, of carcinoma of the nose.

Pittam, Jesse Thomas ✠ Kansas City, Mo.; University Medical College of Kansas City, 1902; an Associate Fellow of the American Medical Association; formerly on the faculty of his alma mater; affiliated with St. Joseph Hospital; died July 6, aged 76, of esophageal hemorrhage.

Pope, George Frederick, Winnemucca, Nev.; Columbia University College of Physicians and Surgeons, New York, 1892; at one time associated with the Indian Service; served during World War I; died July 6, aged 82, of left hemiplegia and cerebral thrombosis.

Porter, Robert Henry Jr., Glasgow, Ky.; Rush Medical College, Chicago, 1901; affiliated with Glasgow Community Hospital; died July 18, aged 76, of arteriosclerosis.

Reed, Mark Eugene, Tonawanda, N. Y.; New York Homeopathic Medical College and Hospital, New York, 1898; died July 6, aged 76, of chronic myocarditis.

Rice, George Arnold ✠ Holden, Mass.; Tufts College Medical School, Boston, 1916; member of the American College of Chest Physicians and the American Trudeau Society; affiliated with Rutland State Sanatorium in Rutland and the Holden District Hospital; died June 8, aged 60, of coronary heart disease.

Richards, William Clifton ✠ Glasgow, Ky.; Hering Medical College, Chicago, 1912; past president of the Barren County Medical Society; on the staff of the T. S. Sampson Hospital, where he died July 30, aged 63, of acute coronary thrombosis.

Ross, Francis Alexander, Ozone Park, N. Y.; Long Island College of Medicine, Brooklyn, 1940; served during World War II; died July 5, aged 41.

Salomonski-Rosen, Moritz ✠ New York; Universität Leipzig Medizinische Fakultät, Saxony, Germany, 1905; affiliated with Mount Sinai Hospital; died in St. Luke's Hospital July 11, aged 72, of myocardial insufficiency.

Schloemer, Adolph J. ✠ Menomonee Falls, Wis.; Marquette University School of Medicine, Milwaukee, 1921; died in Rockfield June 12, aged 66, of coronary thrombosis.

Schott, Edward Francis ✠ Lynn, Mass.; Kaiser-Wilhelms-Universität Medizinische Fakultät, Strassburg, Germany, 1909; on the staffs of the Lynn and Union hospitals; died July 6, aged 66, of cerebral hemorrhage.

Schwedenberg, Theodor ✠ Seaford, Del.; Christian-Albrechts-Universität Medizinische Fakultät, Kiel, Prussia, Germany, 1905; died in Peninsula General Hospital, Salisbury, Md., June 24, aged 76, of cerebral hemorrhage.

Scott, S. Horace, Coatesville, Pa.; Jefferson Medical College of Philadelphia, 1889; for many years a member and president of the school board; formerly chief of staff at Coatesville Hospital; died July 13, aged 87.

Sherrill, Rufus Hansen, Broken Bow, Okla.; University of Arkansas School of Medicine, Little Rock, 1915; served during World War I; died July 1, aged 66, of coronary thrombosis.

Skapier, Joseph, New York City; Université de Paris Faculté de Médecine, France, 1936; affiliated with Goldwater Memorial Hospital, where he died Aug. 15, aged 50, of melanoma.

Spelman, Thomas Joseph ✠ New Rochelle, N. Y.; Long Island College of Medicine, Brooklyn, 1941; certified by the National Board of Medical Examiners; specialist certified by the American Board of Surgery; served on the faculty of his alma mater; on the staff of New Rochelle Hospital, where he died July 24, aged 36, of chronic glomerular nephritis.

Stephens, Robert Clarence ✠ Plymouth, Ind.; Missouri Medical College, St. Louis, 1893; an Associate Fellow of the American Medical Association; died in Parkview Hospital June 8, aged 83, of arteriosclerotic heart disease.

Stott, Charles Edward ✠ Albany, N. Y.; Albany (N. Y.) Medical College, 1912; died July 16, aged 66, of cerebral hemorrhage.

Strain, John Edwin, North Bonneville, Wash.; Detroit College of Medicine, 1906; for many years health officer; died in Barnes Hospital, Vancouver, July 3, aged 80, of coronary occlusion.

Sweeney, Edward Edmond, Silver Spring, Md.; University Medical College of Kansas City, 1908; served during World War I; died July 3, aged 78.

Taylor, Thaddeus Arthur ✠ Lufkin, Texas; Memphis (Tenn.) Hospital Medical College, 1901; past president of the Angelina County Medical Society; for many years a member and past president of the board of managers of the Angelina County Hospital; during World War I director of the Red Cross, and at the time of his death member of the appeal board for Selective Service; vice-president of the Guaranty State Bank; died July 17, aged 76, of arteriosclerosis.

Tillman, George Clarence ✠ Clearwater, Fla.; Atlanta Medical College, 1914; member of the Southeastern Surgical Congress; fellow of the American College of Surgeons; past president of the Florida Railway Surgeons' Association; affiliated with Morton F. Plant Hospital, where he died June 29, aged 61, of coronary thrombosis.

Tingley, Louisa Paine ✠ Boston; Tufts College Medical School, Boston, 1901; member of the American Academy of Ophthalmology and Otolaryngology and the New England Ophthalmological Society; fellow of the American College of Surgeons; ophthalmologist, New England Deaconess and Massachusetts Women's hospitals; consulting ophthalmologist, Palmer Memorial Hospital; died July 16, aged 83, of coronary thrombosis.

Totten, Evan Churchill ✠ Madison, Ind.; Medical College of Ohio, Cincinnati, 1900; died June 2, aged 77, of congestive heart failure.

Travis, Finis Mace ✠ Frankfort, Ky.; University of Louisville Medical Department, Louisville, 1907; member of the state board of health; died in Lexington July 2, aged 69, of uremia and carcinoma of the prostate.

Venable, Wade Hampton, Chatham, Va.; University of Virginia Department of Medicine, Charlottesville, 1889; formerly a Presbyterian medical missionary in China; died in Danville July 9, aged 85, of arteriosclerotic heart disease.

Vinton, Luther Mansfield ✠ Atlanta, Ga.; Emory University School of Medicine, 1921; also a graduate in pharmacy; member of the American Academy of General Practitioners; received the Selective Service Medal for his work as Selective Service examiner during World War II; for many years on the Fulton County Welfare Board, serving as its chairman in 1950-1951; on the staff of the Crawford W. Long Hospital; died July 2, aged 63, of coronary occlusion.

GOVERNMENT SERVICES

ARMY

Sixty-Fifth General Hospital Reunion at Duke University.—The 65th General Hospital Unit will celebrate its 10th anniversary of call to active duty with a reunion at Duke University, Durham, N. C., Oct. 31 to Nov. 1.

This will be the second reunion since the Duke unit was assigned to active duty in July, 1942. Most of the 170 present and former officers and nurses of the unit are expected to attend. Special guests will be Rev. and Mrs. G. V. Cotton of Rickenhall Rectory, Botesdale, England. The 65th's colors hang in the chapel of Rev. Cotton's church next to a plaque commemorating the unit's work. The 65th spent two years in England, serving as one of the major hospital centers for Eighth Air Force casualties. Since the war the 65th has been established as a permanent Reserve Army hospital unit. Highlight of the program will be an address by Brig. Gen. Rawley Chambers, chief of professional services, Surgeon General's Office, on "Present Day Handling and Care of Casualties in the Korean War."

Festivities will begin with a get-together Friday afternoon and a dinner Friday night. Participants will attend the Georgia Tech-Duke homecoming football game Saturday afternoon, Nov. 1.

Surgical Hospital Treats Fifty Thousandth Battle Casualty.—The 8055 Mobile Army Surgical Hospital, the first of its kind in Korea, has just treated and evacuated its fifty thousandth battle casualty. The 200 bed hospital, organized two weeks after the outbreak of the Korean war, has been at its present location, just behind the front lines, since last October. Helicopters and ambulances have brought in wounded United Nations troops. Hospital personnel take pride in the amazing patient recovery rate of 99.8%. Major Jeremiah Holleman, MC, Columbus, Miss., heads the staff of 15 American and Canadian physicians, 1 American dentist, 16 nurses, and 181 other officers and enlisted men assigned to administrative and technical duties. The nursing staff, under Capt. Lorena M. Goodell, Army Nurse Corps, Syracuse, N. Y., includes nurses from the Netherlands, France, Greece, and the United States.

Prisoners to Receive Awards.—About 125 prisoner volunteers at Stateville Prison, Joliet, Ill., will receive Certificates of Achievement issued by the Office of the Army Surgeon General for "participation in experiments on the prevention and cure of malaria." The certificates, signed by Major Gen. George E. Armstrong, MC, Army Surgeon General, and Col. John R. Wood, MC, chairman of the Army Medical Research and Development Board, will be presented to the prisoners by Dr. Alf S. Alving of the University of Chicago. Dr. Alving has directed toxicity studies and clinical investigations of primaquine, (*J. A. M. A.* **149:**1558 [Aug. 23] 1952) the new antimalarial drug, and other promising compounds at the prison for both the United States Public Health Service and the Army Medical Service since Jan. 1, 1950.

Korea Society News.—Dr. Charles M. Wheeler of the public health and welfare medical section of the Far East Command read a paper on plague at a recent meeting of the X Corps Medical and Dental Society in Korea. Lieut. Col. Philip J. Noel Jr. of Louisville, X Corps surgeon and president of the medical and dental group, presided at the meeting, held at the 8209th Mobile Army Surgical Hospital. Other papers were presented by Lieut. Col. Irvine H. Marshall, Eighth Army chief of preventive medicine, Major C. Worcester, dental surgeon of a U. S. Army division in Korea, and Col. Harry L. Berman, Eighth Army x-ray consultant.

Personal.—Capt. Robert W. Regan, MC, has been assigned as professor of military science and tactics to the State University College of Medicine at Syracuse, ROTC Unit. Concurrent with this assignment he is serving as a resident in internal medicine at the State University Medical Center.

NAVY

Frostbite in Korea.—Less than 50 cases of frostbite among Navy and Marine Corps personnel have been reported from Korea for the 1951-1952 winter season, it was announced by Rear Adm. Lamont Pugh, Surgeon General, who just concluded a world-wide inspection of Naval medical facilities. During the winter season of 1950-1951 a total of 3,017 cases of frostbite were reported from Navy and Marine Corps personnel in Korea. Of this number 2,739 persons had frostbite only while 278 suffered battle injuries in addition to frostbite. Of the persons with frostbite only, 97% were returned to duty and 3% were invalided from the service. Amputations were required for 2.6% of the frostbite only cases. Of the 278 persons who suffered both frostbite and battle injuries 27% required amputations involving one or more extremity. The amputations were attributable to the frostbite alone in 58 of these cases and to both wounds and frostbite in the remaining 16 cases. There were no deaths reported with frostbite listed as the underlying cause of death; however, frostbite was reported as a contributory cause on eight death certificates.

Because of many factors, including the use of the new boot, changes in combat conditions, and constant education, frostbite was a minimal problem during the last winter season (1951-1952). In fact, less than 50 cases were reported from the First Marine Division and most of these were mild.

Guest Lecture Series.—The first guest lecture of the current series sponsored by the Naval Medical School was held Sept. 26, when Dr. Wilburt C. Davison, Dean, School of Medicine, Duke University, Durham, N. C., discussed changes in medical education and care. The guest lecture series is sponsored annually by the Naval Medical School for the purpose of keeping members of the medical department abreast of the latest developments in medical research, treatment, and care. Civilian physicians and their associates within the metropolitan area of Washington, D. C., are invited to attend and participate in the lectures. Lectures are held on the last Friday of the month from September through May each season.

Personal.—Rear Adm. Lamont Pugh, Surgeon General, was the principal speaker Sept. 20, at the golden anniversary of the Naval Hospital Corps School, Portsmouth, Va., which is the oldest of four such schools that the Navy maintains for training its enlisted hospital corps personnel.

VETERANS ADMINISTRATION

Course in Psychiatry and Neurology.—The Veterans Administration is instituting a four month intensive training course in psychiatry and neurology to fit the needs of physicians without such previous training who are assigned to duty in 22 predominantly psychiatric hospitals. Physicians who have been engaged in general practice may request this training on applying for a position at one of these hospitals. The course will be held at the VA Hospitals in Coatesville, Pa.; Palo Alto, Calif.; and the joint Downey-Hines, Ill., program near Chicago. Physicians will be employed at salaries commensurate with their training and experience (salary range: $5,500 to $11,800 per annum) and assigned to the course with travel and per diem for the four month period. Information may be obtained from your nearest VA Hospital or regional office, or by writing to the Chief Medical Director, Veterans Administration Central Office, Washington 25, D. C.

Personal.—Dr. Horace B. Cupp, manager of the Veterans Administration Hospital at Chamblee, Ga., has been appointed manager of the new 491 bed VA Hospital at Durham, N. C., which is scheduled for completion in November, and which will be affiliated with the Duke University School of Medicine.

FOREIGN LETTERS

BELGIUM

International Office of Documentation of Military Medicine.—The 15th session of the International Office of Documentation of Military Medicine took place at Liège and Brussels, June 4-7, 1952, under the honorary presidency of the minister of national defense of Belgium and the acting presidency of General Inspector Dr. Jame, president of the International Committee on Military Medicine and Pharmacy, and General Dr. Limbor, chief of the health service of the Belgian Army. Official delegates were sent by 33 nations and 7 international organizations. At the inaugural meeting Generals Limbor, Jame, and Voncken reviewed the accomplishments of this medicomilitary organization, which dates from 1921, and emphasized the determining influence its labors have had on attempts at humanizing war. The following subjects were discussed.

Limits of the Medical Role in Biological Warfare.—This difficult, complex, and delicate question had been posed at the preceding session of the office, at Vichy, in 1951, where the delegates of 15 nations had expressed their concern over this problem, which profoundly affects medical morals. International inquiry, which had elicited more than 30 replies from 20 countries, had resulted in conclusions tending to separate medical activity concerned with the care of the sick and injured from medical activity devoted to research and experimentation. The results were expounded by Advocate-General J. Constant, professor at the Faculty of Law of Liège, and by General Dr. Voncken, secretary-general of the International Committee on Military Medicine and Pharmacy. The juridical and medical data presented showed that in the present state of legislation there is flagrant disagreement between national laws and the dictates of medical ethics. Thus, in the discovery by a physician of a new destructive agent, for example, his conscience commands him to place it at the service of humanity, while the national law considers the divulgation of the secret to other nations as contrary to the security of the state. It was for the purpose of resolving this difficulty that many replies to the inquiry pointed out the necessity of making a clear distinction between the physician whose mission is to preserve life and the experimental biologist who devotes himself to research involving participation in the preparation of bacterial warfare. Briefly, one can summarize the replies to the inquiry by emphasizing the fact that biological warfare, in which the physician may become involved as a result of experimental research, presents problems of conscience. Comparative study of the various national legislations shows that they are in contradiction with the very principles of medical ethics; resolution of this conflict, which threatens permanent danger to the exercise of the medical profession in time of war, is urgently needed.

One of the solutions contemplated (one which would, however, be precarious) is the separation, even in administration, of the services of care and the services of research, so as to leave to the first the immunities necessary for the organization of medical care. For a satisfactory and definitive solution, an effort must be made to obtain by means of intergovernmental conference international acceptance of the medical statute and provisions for the application of this statute. That would constitute the first practical accomplishment of international medical law. The delegates who took part in the discussion emphasized particularly the definition that should be given to the physician and to the biologist. This definition is the basis of the distinction to be made between the physician in the strict sense of the word and the investigator who cannot claim the status of a noncombatant. The assembly, however, did not wish to take a position formally at present in this serious matter; it insisted on the need for the formulation of general rules in a convention comparable to that of Geneva, embracing all the powers, to fix the position, the rights, and the duties of physicians, creating in sum an international statute for the exercise of the medical profession. This statute would be based on moral rules, international ethics, and medical ethics as they now exist or as they might flow from general agreement. It is toward this end that efforts must be concentrated.

Relief of Medical and Religious Personnel Held as Prisoners of War.—This question, which has already been the subject of numerous works emanating from all army health services, has been resolved in a practical manner, owing to the summary prepared by Physician-in-Chief Puyo. Among the points of interest dealt with in the document are the following: Medical and religious personnel falling into the hands of the enemy are not to be held except as necessitated by the medical requirements, spiritual needs, and number of prisoners. Medical personnel should include 1 physician for each 2,000 prisoners or less, specialists not included, with a reserve of 2 for each 10,000 to replace personnel temporarily incapacitated; 1 pharmacist for each 10,000 prisoners; and 1 dentist and 1 dental technician for each 2,000 prisoners. Surgeons and specialists should not be detained unless their services can be utilized in hospitals attached to camps and then only in the following proportions: 1 surgeon for each 5,000 prisoners, and 1 otorhinolaryngologist, 1 ophthalmologist, 1 psychiatrist, and 1 specialist in tuberculosis for each 10,000. Highly trained specialists, such as neurosurgeons, should not be detained. Every opportunity should be given by the detaining power to the country of the specialist's origin to provide him with all necessary material for the practice of his specialty. Medical and religious personnel of all classes should be relieved at the end of one year, by volunteers if possible, and according to certain priority standards.

Identification of Medical and Religious Personnel in the Armed Forces.—A study of the available information relating to the identification of medical and religious personnel was presented by General Dr. des Cilleuls. The principle of a single insigne for medical personnel was adopted, and the secretariat-general of the IODMM was charged with assembling material on the subject. To carry out the plan, it was decided to open a competition (the rules of which will appear later) to obtain designs for a model of an international insigne to be adopted for medical personnel. It was urged that a special identity card should be adopted and distributed in time of peace and that it should bear an indication of the specialty as well as a number to be communicated to the Red Cross International Committee, in order to facilitate recognition of the status of the card holder as a member of the medical services in all circumstances. The Yugoslav delegate (General Jovanovic) advocated that the protection of the Geneva conventions be extended to medical personnel of every category and that the same identity card be given to all. This motion was supported by Dr. Pierre Glorieux, president of the World Medical Association, who asked that this question of the protection of all physicians without exception be taken up and an appeal be addressed to the International Committee of the Red Cross in this connection. It was decided to put this problem on the study schedule of the next session.

The next session of the IODMM will be held following the 14th International Congress of Military Medicine and Pharmacy, in March, 1953, at Montevideo, at the invitation of the government of Uruguay. This invitation was commented on by M. E. de Arteaga, Minister of Uruguay at Brussels, who was present at the closing session.

The items in these letters are contributed by regular correspondents in the various foreign countries.

DENMARK

Frequency of Hepatitis Among Physicians.—The investigations conducted in Sweden by Strömbeck (*J. A. M. A.* **148:**1442 [April 19] 1952) into the frequency of epidemic hepatitis among physicians has its counterpart in Denmark, where Dr. Sten Madsen has published his findings in *Ugeskrift for Laeger*, July 17, 1952. His comprehensive enquiry was addressed to some 10,000 persons, among them 4,700 physicians, 2,000 lawyers, and a great number of hospital nurses, as well as the employees of three important industrial concerns. These persons were asked if they had suffered from acute hepatitis either before or after the age of 18 years. In every age group there was a statistically significant preponderance of hepatitis among physicians as compared with persons in other professions or occupations. For both physicians and lawyers the hepatitis rate reached its maximum between the ages of 40 and 50, whereas the maximum was reached 10 years earlier by persons with other occupations. In other words, nurses and industrial employees developed the disease earlier than physicians or lawyers. Among the 463 physicians who stated that they had suffered from hepatitis in adult life were 444 who gave supplementary information concerning the sources of infection. In as many as 160 cases, a hospital was said to have been the source of infection, whereas in 100 cases the disease was thought to have been contracted in ordinary medical practice. Altogether the frequency of hepatitis after the age of 18 was 8.4% for physicians, 6.8% for nurses, 7% for lawyers, and 3.9% for industrial workers and employees. No medical specialty appeared to favor the development of hepatitis, and neither laboratory nor postmortem room personnel seemed to be particularly prone to this disease, whose severity, as indicated by the duration of jaundice, increased with age.

The Swedish and Danish investigations of this problem were not conducted on strictly identical lines and did not lead to mutually confirmatory findings in every respect. For example, the Swedish investigation showed some, but not a statistically significant, difference in the incidence of hepatitis among operating hospital physicians and hospital physicians who did not operate. But it is evident that in both countries the hepatitis morbidity is exceptionally high among physicians. Presumably this is so because of opportunities for infection in the course of a physician's work. It is curious that Danish hospital nurses, who come in such intimate contact with their patients' discharges, have a lower hepatitis morbidity than Danish lawyers.

Cramp at Night.—An investigation recently carried out in Denmark with the help of several general practitioners has taught the salutary lesson that we need not always depend on the hospitals for scientific research. The story begins with the publication in 1950 of an article in THE JOURNAL (**142:**1140 [April 15]) by Naide on the treatment of obstinate cramp at night by diphenhydramine (benadryl®) given at bedtime in doses of 50 mg. The success achieved in 17 cases was explained by a reference to the ability of this drug to relax the muscular rigidity of Parkinsonism. This article led Dr. Erik Jacobsen to ask if the Danish equivalent of benadryl® (amidryl) might not be as successful in Danish patients. He also tested the effects of rigidyl (B-diethylaminoethyl benzohydryl ether hydrochloride), which Mogens Fog of Denmark showed in 1950 to have a beneficial effect on the muscular rigidity of Parkinsonism.

Arguing that cramp at night is not common in hospital and that more suitable material could be found in the patients' homes, Dr. Jacobsen invited several general practitioners to cooperate in a carefully planned system of tests. Each patient was to receive from his or her physician 25 tablets, one of which was to be taken every night. Of the three different kinds of tablet, the white tablets contained 50 mg. of amidryl, the yellow tablets 50 mg. of rigidyl, and the red tablets contained only a little coloring matter and served as controls. At the time neither physician nor patient knew which tablet was which. At the end of each test the patient was required to fill in a questionnaire provided by the physician. Among the 56 patients were 37 who had suffered from cramp at night for more than two years, and there were only 4 who had suffered from it for less than six months. In 27 cases a host of other remedies had been tried but with little effect except for the remedies containing morphine. The statistical analysis showed no significant difference between the three tablets, and more than half of the patients taking the control tablets said that they obtained some benefit from them. This suggests that cramp at night runs a much more capricious and unpredictable course than the patient realizes, with intervals of freedom that he is apt to overlook. Three of the patients were free from cramp throughout the three weeks during which they took the control tablets, although they had complained of attacks at night over a long period.

Systematic Examinations for Tuberculosis in School Staffs.—The law of July 12, 1946, provided for examinations for tuberculosis in school staffs every year, tuberculin-negative persons to be tested again with tuberculin, and tuberculin-positive persons to be subjected to radiological examinations. Owing to a report on the subject by Dr. Knud Bojlen, it is now possible to see how far this law has been put into effect in Copenhagen. His report covers a seven year period between the scholastic year 1944-1945 and that of 1950-1951. The medical examinations were extended not only to teachers of both sexes, but also to school physicians, school dentists, the kitchen staffs of schools, and everyone else coming within the school system and in direct or indirect touch with schoolchildren. All who had previously been tuberculin-negative were tested with Mantoux every year, and for those who were found still to be negative BCG vaccination was recommended. The tuberculin-positive persons underwent radiological screening, suspect cases being radiologically examined at even shorter intervals than once a year.

Because of systematically kept records and card indexing, Dr. Bojlen could present a clear birds'-eye view of the subject in his carefully tabulated record. In the first year under review 4,000 persons were examined, and in the last year 5,518. The percentage of tuberculin-positive reactors did not vary much from year to year, being 86.4 in the first year and 84 in the last. But the percentage of BCG-vaccinated persons rose from 1.4 in the first year to 9.9 in the last year. Throughout these seven years a total of 26 persons were found to be suffering from active tuberculosis, i. e., a rate of 0.81 per thousand. In the same seven year period 256 persons were kept under special supervision to watch for tuberculosis. The chief lesson of this report is that by frequent and systematic special examinations for tuberculosis, it is possible to find a certain number of cases of active tuberculosis even in a section of the community that has already been carefully combed in a search for this disease.

ITALY

Untoward Effects of Antibiotic Therapy.—Professor Coppo, director of the University of Modena Medical Clinic, lectured on untoward effects of antibiotic therapy, especially in pulmonary disease. He classified these effects into the following nine groups, seven of which are related to antibiotic therapy in general, while the other two refer to therapy of pulmonary disease.

1. Specific hypersensitivity to the antibiotic, as manifested by allergic dermatoses after administration of penicillin, is often witnessed.

2. Generic intolerance to antibiotics may be of toxic nature, it may be due to Herxheimer's reaction, or it may be of indefinite nature. Among these, according to the speaker, are toxic manifestations due to streptomycin to the second and eighth cervical nerves; manifestations to the latter were seen only in patients with renal tuberculosis. Professor Coppo observed an adult with tuberculous meningitis who finally recovered, but in whom streptomycin injected into the cavity had caused a flaccid paraplegia that disappeared completely after the antibiotic was substituted with amithiozone (thiosemicarbazone). Sometimes it is difficult to distinguish these reactions of toxic origin from encephalitic or myelitic tuberculous complications.

3. Some persons attribute increased blood coagulability to thrombophlebitis from intravenous injection of penicillin, while others insist that it is due to a generic thrombogenic effect of the antibiotics. Others, however, have reported definite and constant prolongation of the coagulation time.

4. Other effects are due to a decreased production or an excess elimination of vitamins and hormones. During administration of antibiotics, inflammation of the lip, tongue, esophagus,

and vagina may occur. These disturbances are due to a deficiency of estrogens or factors of the vitamin B complex. In these cases the antibiotic may act as a specific antivitamin. Therefore, it is necessary to complete the antibiotic therapy with administration of vitamins and hormones.

5. Some effects are due to the activation of microbiological entities competing with those sensitive to the antibiotic and to alteration of the normal processes of immunization. Esophagitis, enteritis, and vaginitis due to Monilia albicans may occur during antibiotic therapy. According to the speaker, this is one of the most interesting and important problems of antibiotic therapy.

6. Specific resistance of the pathogenic agent to the antibiotic increases. The dosages that are today believed to be necessary for the treatment of typical diseases caused by bacteria sensitive to penicillin are much larger than those recommended by Fleming in 1946; an analogous phenomenon has occurred in the field of sulfonamide compounds. It is not, therefore, arbitrary to suspect a quick selection or modification of the microbiological strains, during the last 10 years, due to the influence of antibiotic therapy. In particular conditions of dosage, antibiotic therapy may cause increased resistance of the active pathogenic agent. Professor Coppo stressed the great responsibility that lies in the experimental use of antibiotics, which should be given in normal doses, only for a few days, and with chain substitution of other antibiotics if the patient does not improve. In these cases the pathogenic agent is not eliminated but is changed; the clinical manifestations of the morbid process are also changed. The outcome of the disease may be compromised by therapy that is not carried out well.

7. The pathogenic agent is temporarily concealed during antibiotic therapy. An antibiotic that, for various reasons (dosage, duration of action, and specific effect), is unable to eliminate the pathogenic agent may at the same time cause it to be hidden during hemoculture or bacteriological investigations. This inconvenience, according to the speaker, justifies the hope of solving with adjuvants an obscure diagnosis on the basis of the effect caused by an antibiotic.

8. Suppurative evolution may represent a severe inconvenience in the field of pulmonary pathology. Thus, using inadequate doses of antibiotics, there have been cases, especially during the 1948-1949 influenza epidemic, in which the pneumonic focus of infection changed into an abscess, sometimes associated with empyema.

9. Complications occur in the field of pleuropulmonary pathology, especially in case of a late diagnosis of primary bronchopulmonary cancer. This delay in the exact diagnosis may derive from an apparent recovery of the pleuropulmonary manifestations that sometimes constitute the first sign of the neoplasm.

Eventual Variations of Blood Group.—At a meeting of the medicosurgical society of the Romagna region Professor Bazzocchi described the case of two patients who after "chloronaphtine" therapy apparently altered their blood group, one passing from group O to group A and the other from group A to group AB. The two patients continued to receive, without inconvenience, transfusion of blood of the group to which they belonged before treatment was instituted. Professor Bazzocchi's report aroused an interesting discussion. Professor Battistini believes that, on the basis of our present day knowledge, a mutability of the blood groups cannot be ascertained. It is probable that "chloronaphtine" determined some humoral modifications that had an effect on the phenomenon of agglutination, inhibiting or delaying it. He suggested some technical devices to study this hypothesis. Professor Cavina pointed out that some abnormal phenomena of agglutination may be interpreted as alterations of the plasma proteins.

While Professor Babini doubted the possibilities of changing the blood groups, Professor Zoli conceded that phenomena like those described by Professor Bazzocchi can occur and their explanation can be reached through a deeper study of the physiology of the plasma proteins. In fact, the "naphtochlorines," like other drugs, have a great biological action on the cellular enzymatic processes. Professor De Castro believed that, of the various hypotheses advanced by the speakers to explain the phenomenon described by Professor Bazzocchi, the most reliable was that of alterations of the blood plasma owing to the disease and myelotoxicosis produced by nitrogen mustard. It is not, in fact, exceptional to find quantitative changes of the phenomenon of agglutination of the erythrocytes with respect to quantitative variations of definite types of globulins. The appearance of pseudoagglutinations of erythrocytes attributable to conditions of discolloidity of the plasma is likewise not exceptional. These factors ought to be considered thoroughly by those physicians who, in their transfusions, have occasion to observe conditions analogous to those described by Professor Bazzocchi.

LONDON

Combined Meeting of British and Irish Medical Associations.—*Motorcyclists' Deaths.*—Concern at the number of deaths among motorcyclists through lack of protective headgear was expressed at the combined meeting of the British and Irish Medical Associations, which was held in Dublin, July 3-11. Dr. Teare, the home office pathologist, said many physicians would support legislature to compel motorcyclists to wear crash helmets; meanwhile, he thought motoring association scouts should wear them to set an example. He reported that road traffic accidents cost the country over 400 million dollars last year and commented on the fact that, in the Eighth Army in Africa during the war, deaths from head injuries were halved by the compulsory use of crash helmets. It should be compulsory to sell crash helmets with motorcycles. Analyzing deaths of persons between 14 and 55, Dr. Teare said those of pedestrians were fewest. "They are more sprightly between these ages."

Suicides.—In discussing coroners' autopsies that he had performed, Dr. Teare said that out of 2,078 in the age group 15 to 44 unnatural causes accounted for 859 deaths, and suicide headed this list, causing deaths of 183 men and 131 women. More than one-third of these deaths were due to coal gas poisoning. There was also a mounting tendency among women to use barbiturate drugs. The figures for suicide by shooting were 14 men and no women. Abortion accounted for many deaths, the fear of another child in an already overcrowded home often being the cause.

Pertussis Immunization.—At a discussion on immunization, Dr. Parrish spoke of the possibility of successful immunization against pertussis and foreshadowed a country-wide campaign in Britain. Dr. Meenan said that new anti-influenza viruses had been developed and were ready for trial. As a result of recent development, immunization against poliomyelitis was within the bounds of possibility.

Fatigue.—The Army's method of dealing with exhaustion and fatigue caused by hot weather was described by an Army physician. "Years ago, in India, when we played hard games, our method was to take a gin and ginger-beer with a teaspoonful of salt in it to overcome the feeling of fatigue."

Cortisone.—Differences of opinion among physicians concerning cortisone were evident in the discussion by members of the British and Irish Medical Associations. On the question, "Is it a wonder drug or just a glorified aspirin?" Prof. R. H. Micks of Dublin said, "There is no evidence yet that it lowers the death rate in acute rheumatic carditis." But Prof. H. Moore, chairman of the cortisone committee of the Medical Research Council of Ireland, said that he believed the use of cortisone could save the heart in cases of rheumatic fever. Prof. D. K. O'Donovan of Dubin said there was a popular belief that cortisone only masked the symptoms and did not cure. "That may be true in a strictly pathological sense, but it should be more widely known that it is a curative drug by the ordinary reasonable standards of cure." Dr. Schlesinger of London said the drug could not yet be decontrolled and made generally available to the public. There had been many remarkable recoveries in desperate cases, but his experience so far had not convinced him that it was a cure. Professor Moore announced that Ireland had received a gift of 40 thousand dollars' worth of cortisone from an American firm. The Irish Minister of Health was considering a scheme for free distribution to patients who were not able to pay for it.

CORRESPONDENCE

STANDARDS FOR THE CARE OF POLIOMYELITIS RESPIRATOR PATIENTS IN NEW YORK

To the Editor:—I would like to bring the following statement to your attention, since we understand that the material is unique and we thought it might be of interest to the readers of THE JOURNAL. The problem of the patient with poliomyelitis needing care in a respirator is complicated and has presented difficulties in many areas, including New York City. It was for this reason that these standards, now officially approved by the New York City Department of Health, were developed.

STANDARDS FOR THE CARE OF POLIOMYELITIS RESPIRATOR PATIENTS IN NEW YORK CITY

The material contained in this set of standards has been developed by the Bureau for Handicapped Children of the New York City Department of Health with the assistance of a technical advisory committee of which Dr. Rustin McIntosh is chairman. This material is intended for use as a general guide in the development of respirator centers in New York City.

It is recommended that there be established in the City of New York one or more centers for the treatment of patients with respiratory difficulty caused by poliomyelitis, hereinafter designated as the center; that this center be so organized that it will: (*a*) provide treatment for patients in the acute phase of poliomyelitis; (*b*) provide treatment for poliomyelitis patients who still suffer from respiratory difficulty one month or longer after onset of poliomyelitis.

This plan implies that no attempt will be made to provide care for all patients with respiratory difficulty during the acute phase of poliomyelitis, but that an attempt will be made to provide treatment for all poliomyelitis patients who, after one month's illness, still require hospitalization for respiratory difficulty.

It is recommended that, at least in the beginning, a unit designed to care for 12 patients be established. Experience indicates that this is the smallest number of patients that can be cared for with maximum efficiency and economy. The 12 patients in the unit will require the bed space generally used in hospitals for 24 patients because of the nature of the equipment which is used for their care.

It is recommended that the center be established at and in connection with a general hospital since the complexity of the problem presented by poliomyelitis patients with respiratory difficulty requires the services of specialists in many fields.

Medical Staff.—[There should be] a fulltime director of the center. The director should be an internist or a pediatrician with experience in the care of poliomyelitis patients and preferably with special training in physiology. Training in administrative duties would be very valuable. The director should act in the capacity of physician-in-chief. He should be personally charged with the care of the patients. He should be responsible for the establishment of general policies as well as for the technical procedures carried out. He should be the coordinator of all the activities carried out in the center, and the final decision regarding recommendations made by his staff should rest with him.

[There should be] a fulltime assistant director. Experience has shown that the care of patients with chronic respiratory difficulty caused by poliomyelitis requires the attention at all times of an experienced physician. These patients frequently require emergency treatment which demands the presence of a physician experienced in dealing with such emergencies. A fulltime assistant director in addition to the director is therefore necessary in order to provide the presence of an experienced physician at all times. This person might be a clinical fellow on a yearly basis, under the director of the center.

The training of the assistant director should complement that of the director; for example, the director might be an experienced internist or pediatrician while the assistant director might be a person trained specifically in physiology or anesthesiology. The assistant director should act as assistant to the director and stand in the latter's place during his absence.

A resident or intern from the pediatric or medical service of the general hospital should be assigned to the center. The care of patients in the center should be constantly provided for in the same manner as in the general hospital insofar as assignment of house officers is concerned.

A physiologist or anesthesiologist . . . is essential [for] the center. . . . He need not be a fulltime member of the staff but he should be a staff member of the general hospital to which the center is attached. He should be specifically assigned to duty in the center.

A qualified orthopedist who is especially interested in the care and rehabilitation of patients with poliomyelitis should be placed in charge of the orthopedic work of the center. He should be assisted by at least one qualified orthopedist. A resident orthopedist on the pediatric service of the general hospital should be assigned to the center as part of his regular duties. A qualified physiatrist with special interest in rehabilitation should direct the physical therapy at the center. A resident or fellow in physical medicine on the staff of the general hospital should be assigned to the center.

An otolaryngologist with experience in bronchoscopy should be on the staff of the center. He should be assisted by at least one other physician with similar training. One of these two men should be on call at all times for emergency work in the center. A resident from the otolaryngological service of the general hospital should be assigned to the center as part of his regular duties and one such resident should be on call at all times for work in the center.

A qualified psychiatrist from the staff of the general hospital should be assigned to the center. He should be assisted by at least one other well-trained psychiatrist. A resident psychiatrist from the staff of the general hospital should be assigned to the center as part of his regular duties. It is important that one of the two psychiatrists interview each patient on entrance or as soon after entrance to the center as possible and that necessary psychotherapeutic steps be taken as soon as possible. Psychiatrists assigned to the center should be assisted by psychologists and should be reponsible for conducting staff orientation and education of all the staff assigned to the center.

Nursing Staff.—The nursing staff of the center should be organized as a group or unit. This unit should have the same relationship to the nursing staff of the general hospital as does the staff of any other unit within the hospital. The nursing staff of the center should be organized in the following manner:

(*a*) A supervising nurse or nurse-in-charge should be a registered nurse and should be responsible for the overall nursing care which is carried out in the center. She should be a person who has had special education and experience in the care of respirator poliomyelitis patients.

(*b*) An assistant supervising nurse with qualifications similar to those of the supervising nurse. The supervising nurse or her assistant should be on duty in the center at all times.

(*c*) A head nurse for each tour of duty. She should be a registered nurse and should have special education and experience in the care of poliomyelitis patients.

(*d*) The following nurse-patient ratios are suggested: For acute respirator patients—one member of the nursing team consisting of one registered nurse assisted by a practical nurse or aide, and for each 3 patients on each tour of duty. For patients whose respiratory status is not critical, i. e., in general, those patients who have passed through the acute phase of the illness and who are suffering from respiratory disability of static nature or of relatively minor character—one member of the nursing team consisting of one registered nurse assisted by a practical nurse or aide—for every 5 patients on each tour of duty.

(*e*) All nursing and auxiliary personnel assigned to the center should work under the supervision of a registered professional nurse at all times. It is recommended that members of the nursing as well as the auxiliary staff receive an initial period of instruction prior to assignment to the center.

(*f*) There should be a staff of male attendants on duty at all times in sufficient numbers to assist in the performance of the manual labor often required in the handling of heavy apparatus used for the care of poliomyelitis respirator patients; at least one attendant for every 4 patients in the acute stage and one attendant for every 6 patients suffering from respiratory disability of static or relatively minor character.

(*g*) Student nurses and medical students should be assigned for teaching purposes only.

[There should be] one qualified physical therapist for every 5 patients in the center. For a center having 12 respirator patients, 2 physical therapists should be provided. The physical therapists should be under the direct supervision of the physiatrist and his assistant.

An occupational therapist should be assigned to work in the center under the direct charge of the director of the center who, with the assistance of the physiatrist and psychiatrist, will direct and guide his work as regards particular patients under occupational therapy.

The center should have one qualified social service case worker. The work of this case worker should be under the supervision of a qualified social work supervisor attached to the general hospital.

A teacher should be provided for the education of children in the center. There should not be more than 10 children assigned to the teacher. Provision should be made for adult education. It is recommended that the work of this teacher be responsible to the director.

Engineering and Maintenance Staff.—The general engineering problems of the center should be under the supervision of the chief engineer of the general hospital. The maintenance and engineering staff of the general hospital should be increased by one above its usual number, and this member should be assigned the responsibility for all technical and engineering problems which arise in the center during his tour of duty. Relief should be provided for him from the maintenance and engineering staff of the general hospital. There should be on duty at all times for immediate service in the center one maintenance and engineering employee who is thoroughly familiar with the apparatus and electrical circuits in the center. All mechanical equipment in the center should be checked thoroughly daily by the engineering and maintenance employee described above.

Laboratory Personnel.—It is recommended that the routine bacteriologic and chemical determinations required for the care of patients in the center be done by the personnel of the laboratories of the general hospital. In addition, it is recommended that one specially-trained and qualified technician be assigned for full-time duty in the center for such highly specialized determinations as oxygen saturation and pH of blood, estimation of vital capacity, maximal breathing capacity, etc. One dietician from the staff of the general hospital should be charged with the responsibility of providing for the dietary needs of the center.

A fulltime secretary should be attached to the center.

Policy for Admission of Patients.—There will be admitted to the center patients with serious chronic respiratory difficulty following poliomyelitis, as well as patients with serious respiratory difficulty who are in the acute phase of the disease. The director of the center will be responsible for the admission of patients and it is recommended that his decision regarding the eligibility of particular patients for admission to the center be final.

It is recommended that a group of experts be appointed to serve as consultants regarding the advisability of transferring patients in other hospitals to the center; the director of the center should be a member of this consulting group. It is recommended that these experts be paid an adequate consultation fee for their services, the funds to come from an appropriate source.

It is recommended that the center continue to give assistance . . . in the home management of patients who have been discharged from the center. This function . . . should be carried out under the direct supervision of the director or his assistant.

Physical Arrangement.—The center should be a separate but integrated unit, located on one or more floors within the general hospital. It is estimated that approximately 150 sq. ft. of floor space per patient is required. Each room and ward should have running water equipped with foot or knee control, soap or an equally effective detergent, and disposable towels. The arrangement of the rooms and wards should be such as to allow the most practical group care of patients.

In addition to patients' rooms, the center should have: (1) Nurse's station and chart room. (2) Adequate storage space. (3) Facilities for tracheotomy, bronchoscopy and similar procedures. (4) A kitchen or pantry equipped with dishwasher, stoves, refrigerators, etc. (5) A utility room for proper disposal of excreta and for sterilization of bedpans, urinals, etc. (6) Laboratory. (7) Space for physical therapy, occupational therapy and recreation.

Equipment and Facilities.—It is recommended that the center be equipped with the most modern and effective instruments and apparatus used in diagnosis and treatment of patients with respiratory difficulty caused by poliomyelitis. A partial list of such equipment follows:

1. A tank respirator and 1 rocking bed for each patient.
2. One chest respirator for each 3 patients.
3. Eight electric outlets for each patient on 2 electric circuits.
4. One electric suction machine for each 2 patients.
5. Two emergency ENT or OR sets for tracheotomy and bronchoscopy suitable for adults, and 2 sets for infants and children.
6. An adequate number of wheelchairs and stretchers.
7. Equipment for physical therapy, occupational therapy, education and recreation.
8. Utensils for each patient to be kept at his bedside (bedpan, urinal, basin, etc.)
9. One electrophrenic respirator.
10. One fluoroscopy unit.
11. One oximeter with earpieces capable of use on infants, older children and adults.
12. Equipment for washing and sterilizing dishes, bedpans, etc.
13. Laboratory equipment for measurement of breathing capacity, oxygen and carbon dioxide content of blood, etc.

Staff Conferences.—Weekly conferences of the staff should be held to discuss and evaluate the status and progress of the patients in the respirator center. Such conferences should be conducted by the physician-in-charge of the respirator center, and attended by all personnel connected with the respirator center.

Policies and Procedures.—Caps, masks and gowns are not necessary for the chronic patient. There should be careful handwashing before and after handling each patient and between patients.

Dishes may go to the general kitchen. If dishes are washed in a mechanical washer, no particular precaution need be taken; if washed by hand, it may be advantageous to set them aside and wash other dishes first. The recommended procedure is the use of soap or detergent in washing, rinsing in boiling water, and allowing to dry in air. Left-over foods may be scraped off the dish into a paper bag which should be tied and disposed of with the other garbage. Liquid foods may be emptied into a toilet or hopper. All stools may be emptied into a water-flushed, sewers-connected toilet without further treatment. Bedpans should be sterilized after each use.

Complete and detailed records should be kept on each patient including admission history, admission and periodic physical examination, laboratory data, reports of all consultations, evaluation of progress. Prior to discharge home, there should be a report of home conditions and plan for care at home.

All employees assigned to the respirator center should have a preemployment and annual physical examination, including chest x-ray. When an employee develops a disease in a communicable form (respiratory, gastrointestinal, skin, etc.) he should report to the hospital's employee health service. He should be excluded from assignment to the respirator center until certified by a physician that he is free from disease in a communicable form. Special attention should be paid to protection of patients from upper respiratory infections.

Prior to discharge home, referral should be made to a public health nursing agency to assure adequate home conditions and to assure adequate care at home. Prior to discharge home, a plan should be made with the family for whatever ongoing medical care and supervision are necessary.

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USE OF WATER IN HYSTEROSCOPY

To the Editor:—In "Hysteroscope in Diagnosis of Pathological Conditions of Uterine Canal" by W. B. Norment in THE JOURNAL, March 15, 1952, page 917, an ingenious method of visualizing the uterine canal and of taking biopsies under direct vision is described. The promise of improved visual and pathological diagnosis of intrauterine disease, particularly early cancer, by this method is most impressive.

There is one feature of the technique described that is potentially dangerous, that is, the water flow through the uterine cavity. If water were aspirated into uterine veins, intravascular hemolysis might occur, as in transurethral resection of the prostate when water was used for irrigation. The hysteroscope method provides possible avenues of water aspiration in "the slight trauma caused by the outer sheath entering the uterine canal" (page 919) and in the biopsy itself. Apparently, bleeding is frequent and is, indeed, one of the reasons why the water flow is necessary to provide clear vision. To avoid the risk of producing hemolysis, I would suggest using an isotonic fluid such as those that have now universally replaced water in the practice of prostatic resection.

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To the Editor:—Dr. W. B. Norment, in his "Hysteroscope in Diagnosis of Pathological Conditions of Uterine Canal," in THE JOURNAL, March 15, 1952, page 917, has presented a method of uterine canal visualization that not only is simple but, like all other endoscopic examinations, will make the task of the conscientious diagnostician easier and will add years of life to those women who will be inevitably afflicted with cancer of the uterus.

It is rather ironic that medical science has developed techniques for endoscopic examinations of some of the more difficult recesses of the body, such as the bronchus and stomach, long before a technique was devised for the uterine canal, which is unquestionably more easily accessible. More ironic is the fact that we also have means of visualizing the outer surface of the uterus. There is no question that the hysteroscopic examination will achieve its pinnacle of success in the diagnosis of uterine cancer, especially the early and small lesions. This will be an achievement of diagnostic accuracy such as neither has been nor can be obtained by the Papanicolaou, suction biopsy, or curettage methods. Since the goal of the general practitioner, the specialist, and oncologist is an early diagnosis of cancer, it seems to be a waste of ingenuity to use this diagnostic technique only after a hysterogram has revealed a filling defect. It is a distinct possibility that the small lesions, the ones that are most difficult to diagnose, may not produce any filling defect. With the extended use of this technique and especially in the younger woman, where one can even foresee the possibility of fallopian tube catheterization, it is imperative that the retrograde passage of organisms, malignant cells, and "viable" endometrium be further studied and evaluated.

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CORTICOTROPIN AND SUBACROMIAL BURSITIS

To the Editor:—The paper "Corticotropin (ACTH) in the Treatment of Acute Subacromial Bursitis," by Drs. Steinberg and Roodenburg in THE JOURNAL, Aug. 16, 1952, page 1458, is of considerable interest to me. Having had the opportunity to see many patients with this disease, I would be happy if any form of treatment could be found that is uniformly successful. I feel, however, that any such conclusions are unwarranted on the basis of the six cases reported or on the basis of the previous publications by Hollander and others, quoted by the authors.

From our experience, the course of this disease is somewhat like this: As calcium accumulates in the diseased tendon, which may occur in a matter of a few days, the tendon sheath will be under tension and the patient will experience severe pain. In many acute cases, the tendon ruptures and the calcareous material is discharged into the bursa. Coinciding with this event, the acute pain usually ceases or diminishes rapidly. Any therapeutic agent employed at this opportune moment is apt to receive credit for the very dramatic relief that the patient may experience. We discovered this in the course of a study to assess the results of radiation therapy. Much to our surprise, patients who received sham x-ray therapy, in which a thick lead filter was used, preventing all possible radiation from reaching the patient, experienced some of the most dramatic relief.

In the interest of our patients, it would be desirable to subject a group of patients large enough to be statistically significant to corticotropin therapy and to treat an equally large unselected control group by means of placebos. Only then can any conclusions be drawn regarding the effectiveness of a form of therapy in an essentially self-limited disease.

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ZINC PEROXIDE—USEFULNESS AND DANGEROUS PROPERTY

To the Editor:—Meleny has recently assessed the present usefulness of zinc peroxide as a topical medicinal agent (Meleny, F. L.: Present Role of Zinc Peroxide in Treatment of Surgical Infections, *J. A. M. A.* **149**:1450-1453 [Aug. 16] 1952). I agree entirely with his statement that, in spite of the availability of a wide variety of potent antibacterial agents, there are some types of infection of the skin and subcutaneous tissues in which zinc peroxide, and other local medicaments as well, still have considerable usefulness. In addition to the specific types of infection mentioned by Meleny, which fortunately are uncommon, zinc peroxide is often very useful as a deodorant, as has been observed by many. In long-standing exfoliative processes, particularly in moist thickened areas, and in various types of extensive bullous eruptions, a zinc peroxide lotion will often reduce the odor to a tolerable level. Fortunately, as Meleny points out, zinc peroxide in almost any concentration is well tolerated by the skin and subcutaneous tissues.

I would like to add one word of caution. Great care should be exercised to prevent zinc peroxide water suspensions from being dispensed in screw-top containers. If the zinc peroxide is active, such containers will almost certainly explode in time. I have seen this occur on three occasions; fortunately no one was near the bottle in any of these instances. The thorough spattering of the room or cabinet with small bits of glass and lotion attested to the force of the explosion. Cotton-stoppered flasks or wide-mouthed cork-stoppered bottles are quite safe, though the patient should be instructed not to insert the cork too firmly.

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HYPOTHYROIDISM AND GERIATRICS

To the Editor:—In THE JOURNAL, June 14, your leading editorial discussed "Hypothyroidism, a Geriatric Problem." The inferences made at the beginning of the second paragraph: "The basal metabolic rate changes appreciably with aging because of diminished needs of the organism," requires elaboration. In the clinical sense, the term basal metabolic rate is comparative and is based on derviations from an accepted average oxygen consumption duly related to age, sex, height, and weight. With advancing age, there is no question that there is a decreasing rate of oxygen consumption per unit body surface area, but, since this decrease occurs universally, the average relating to the age shows a proportionate change; hence the basal metabolic rate is essentially unchanged. Any decrease in basal metabolic requirements beyond that evidenced by the average for the age group is reflected as a change in the basal metabolic rate.

The occurrence of myxedema in any age group requires corrective therapy. Myxedema is frequently associated with premature senile changes. However, to confuse the decreasing oxygen requirements of the aging population with decreasing basal metabolic rate is not justified by our present definitions.

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equally effective detergent, and disposable towels. The arrange-

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COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

CORRECTION

Internships and Residencies.—The following approved programs were incorrectly listed in the Internship and Residency Number (*J. A. M. A.*, vol. 150, no. 4 [Sept. 27] 1952). It is suggested that these corrections be appended to the lists of approved programs previously published in the Internship and Residency Number. The data for these programs should have appeared as follows:

Internal Medicine

(page 310)

Mercy Hospital [1-3]	Chicago	G. F. O'Brien	1,619	26,880	116	41	2	4	25
Michael Reese Hospital [1-3,15]	Chicago	D. Rosenberg	1,982	30,127	132	68	3	10	25
Woodlawn Hospital [1-3]	Chicago	W. DeYoung							
		F. Shaffner	1,877	347	105	64	1	1	150
St. Francis Hospital [1-3]	Evanston, Ill.	M. W. Sbertoli	2,515	4,448	228	121	2	6	150
Little Company of Mary Hospital [1-3]	Evergreen Park, Ill.	W. J. Hagstrom	3,383	...	..	..	3	3	175
West Suburban Hospital	Oak Park, Ill.	J. C. McMillan	1,618	1,077	265	107	2	2	150
St. Francis Hospital [1-3]	Peoria, Ill.	H. A. Warren	3,055	24,916	314	104	1	2	100
Clinic Hospital [1]	Bluffton, Ind.	A. C. Nickel	1,870	...	44	27	1	6	200
Indianapolis General Hospital [1]	Indianapolis	P. Fonts	1,583	25,077	299	125	4	12	160
Indiana University Medical Center [1]	Indianapolis	J. O. Ritchey	2,309	10,542	174	115	3	7	150
Methodist Hospital [1-3]	Indianapolis	B. D. Rosenak	2,689	6,827	308	69	2	5	260
St. Vincent's Hospital [1]	Indianapolis	R. M. Vandivier	1,358	5,457	173	79	1	3	250
St. Elizabeth Hospital [1]	Lafayette, Ind.	R. A. Flack	3,381	4,108	208	52	1	3	150
Ball Memorial Hospital [1-3]	Muncie, Ind.	C. A. Ball	1,230	...	184	30	2	6	100
Iowa Methodist Hospital [1-3]	Des Moines, Iowa	C. A. Sones	2,412	...	163	74	2	4	100

Obstetrics and Gynecology

(page 320)

Meadowbrook Hospital [1-3]	Hempstead, N. Y.	E. F. Miller	OB	1,198	3,125	1	2	1	200
Mary Immaculate Hospital [1-3]	Jamaica, N. Y.	J. V. Rizzi							
		J. P. McManus	OB	2,472	3,519	1	1	1	110

(page 321)

State University of New York Medical Center [1-3,82]	Syracuse, N. Y.	E. C. Hughes	OB	6,630	5,386	4	16	3	150
		C. E. Clark	GYN	1,855	3,420	2	8	3	150
Charlotte Memorial Hospital [1-3]	Charlotte, N. C.	W. Z. Bradford	OBG	2,514	1,988	1	2	2	150
Duke Hospital [1-3]	Durham, N. C.	B. Carter	OBG	3,249	16,486	3	10	3	25
Watts Hospital [1]	Durham, N. C.	E. B. Easley	OB	1,494	3,656	1	1	1	75
Rex Hospital [1-3]	Raleigh, N. C.	R. J. Ruark	OBG	3,094	2,031	1	1	2	225
North Carolina Baptist Hospital [1]	Winston-Salem, N. C.	F. R. Lock	OBG	2,475	5,105	2	5	3	41.66
St. Luke's Hospital	Fargo, N. D.		OBG	1,820	22,500	2	2	1	300
City Hospital [1-3]	Akron, Ohio	D. C. Snyder	OBG	6,287	2,820	3	6	3	200
Peoples Hospital [1,15]	Akron, Ohio	L. DaSet	OBG	4,286	1,274	2	5	3	225
St. Thomas Hospital [1-3]	Akron, Ohio	H. H. Gibson	OBG	3,041	1,660	2	8	2	200
Mercy Hospital [1-3]	Canton, Ohio	R. K. Ramsayer							
		L. E. Leavenworth	OBG	3,534	95	1	3	2	200
Bethesda Hospital [1-3]	Cincinnati	R. Bryant							
		R. W. Eddy	OBG	4,241	...	2	4	3	200
Cincinnati General Hospital [1-3]	Cincinnati	S. Garber	OB	3,821	6,328	4	5	3	...
City Hospital [1-3]	Cleveland	A. E. Bennett	OB	2,469	8,596	2	7	3	84
			GYN	453	5,284	..	..	1	84
Fairview Park Hospital [1-3]	Cleveland	E. D. Saunders	OB	2,670	238	3	3	1	100
Lutheran Hospital [1-3]	Cleveland	R. S. Dial	OB	2,081	...	1	2	2	162.50
Mount Sinai Hospital [1-3]	Cleveland	L. H. Biskind	OBG	3,493	6,529	1	5	3	215
St. Ann's Maternity Hospital [3]	Cleveland	M. B. Laven	OB	2,083	765	3	3	1	300
St. John's Hospital [1-3]	Cleveland	M. E. Crawford							
		J. E. Morgan	OBG	3,155	66	2	5	2	135
St. Luke's Hospital [1-3]	Cleveland	C. T. Hemmings	OBG	4,610	3,059	1	4	3	100
University Hospitals [1-3]	Cleveland	G. J. Vosburgh	OBG	7,351	25,837	6	14	3	25
Mount Carmel Hospital [1-3]	Columbus, Ohio	R. F. Daly	OB	3,381	870	1	3	2	225
St. Ann's Maternity Hospital [3]	Columbus, Ohio	J. M. Gallen	OB	2,503	525	2	4	2	150
University Hospitals—									
Ohio State University Hospital [1-3]	Columbus, Ohio	A. C. Barnes	OBG	4,100	13,804	2	8	3	125
White Cross Hospital [1-3]	Columbus, Ohio	W. M. Silbernagel	OB	2,922	...	1	2	2	275
Good Samaritan Hospital [1-3]	Dayton, Ohio	J. K. Hoerner	OBG	2,148	818	2	5	2	250
Miami Valley Hospital [1-3]	Dayton, Ohio	R. C. Doan	OB	4,962	1,478	..	1	1	125
Huron Road Hospital [1-3]	East Cleveland, Ohio	J. J. Woodworth	OBG	4,508	114	2	4	3	210
Lakewood Hospital [1-3]	Lakewood, Ohio	B. Wylie	OB	2,037	33	2	2	1	110
St. Rita's Hospital [1-3]	Lima, Ohio	V. A. Noble	OB	2,087	15	1	2	2	175
Maumee Valley Hospital [1-3]	Toledo, Ohio	S. D. Zuker	OB	516	296	1	1	1	210
Mercy Hospital [1-3]	Toledo, Ohio	R. C. King	OBG	3,903	1,191	2	6	2	150
St. Vincent's Hospital [1-3]	Toledo, Ohio	M. W. Diethelm	OBG	3,435	...	2	4	3	200
Toledo Hospital [1-3]	Toledo, Ohio	O. E. Todd	OBG	3,775	1,209	1	3	3	200
St. Elizabeth Hospital [1-3]	Youngstown, Ohio	A. J. Brandt	OBG	4,035	477	1	3	2	200
St. Anthony Hospital	Oklahoma City	G. Rogers	OBG	5,511	3,805	1	3	3	150
University Hospitals [1-3]	Oklahoma City	J. B. Eskridge							
		J. Kelso	OBG	2,570	11,957	1	3	3	75
Wesley Hospital [1-3]	Oklahoma City	J. W. Records	OBG	2,911	3,614	1	1	2	150
St. John's Hospital [1]	Tulsa, Okla.	W. F. Thomas	OBG	3,736	...	3	3	2	150
Emanuel Hospital [1-3]	Portland, Ore.	C. Fearl	OBG	6,924	...	1	3	3	85
St. Vincent's Hospital [1-3]	Portland, Ore.	M. S. Sichel	OB	2,411	...	1	1	1	150
University of Oregon Medical School Hospitals and Clinics [1-3]	Portland, Ore.	H. C. Stearns	OBG	1,416	6,978	1	3	3	85

Otolaryngology

(page 331)

Children's Hospital [1-3]	San Francisco	R. C. Martin	1,110	1,651	1	1		75
San Francisco Hospital [1-3]	San Francisco	L. F. Morrison						
		R. E. Ashley	500	...	..	1		175

Surgery

(page 357)

Jefferson Hospital [3]	Roanoke, Va.	A. P. Jones	3,169	8,513	43	20	1	4	175

COUNCIL ON NATIONAL EMERGENCY MEDICAL SERVICE

The Council has authorized publication of the following statement. C. JOSEPH STETLER, *Secretary.*

STATUS OF U. S. PUBLIC HEALTH OFFICERS UNDER THE "DOCTOR DRAFT LAW"

Recently the United States Public Health Service reverted from a military to a civilian organization. This change affected the status of physicians in the U. S. Public Health Service under Public Law 779, 81st Congress, now incorporated in the Universal Military Training and Service Act, as amended. Part 1 of Information Bulletin, no. 10, volume 3, quoted below was issued on Aug. 12, 1952, by the National Advisory Committee to the Selective Service System to clear this situation.

"The Public Health Service Commissioned Corps, active or inactive, are no longer on a military status. This means that all Reserve Officers of that Corps who are physicians, dentists or veterinarians, under 51 years of age, must now register with their Selective Service local boards under Public Law 779—now incorporated in the Universal Military Training and Service Act.

There is no other change in their status. (1) They are not subject to induction. (2) They receive credit for service the same as the Armed Forces. (3) They receive the $100 a month incentive pay. (4) They get credit for all service rendered after Sept. 16, 1940.

Officers of the Regular Corps do not have to register as special registrants. Special registration is required only of the U. S. P. H. S. Reserve Commissioned Officers Corps, active or inactive, and then only if they are physicians, dentists or veterinarians under 51 years of age."

MEDICAL MOTION PICTURES

Infiltration Anesthesia in the First Stage of Labor: 16 mm., color, sound, showing time 17 minutes. Prepared by Archie A. Abrams, M.D., Assistant Professor of Clinical Obstetrics, Boston University School of Medicine, Boston. Produced in 1951 by Mervin LaRue, Inc., Chicago. Procurable on loan from Eli Lilly & Co., Indianapolis.

This film presents by means of models and animation the causes, sites, and routes of transmission of the pain of labor. The work of Weiss and Davis on the mechanism of peripheral blockage of visceral pain by the use of infiltration anesthesia is illustrated. After a discussion dealing with pain perception being impeded by the action of anesthetic drugs at various points in the body, the infiltration of T-11 and T-12 skin areas to block labor pain, as suggested by David Rose in 1928-1929 and further developed by Abrams, is demonstrated. Using patients in labor, intradermal injections of a 1.5% solution of piperocaine (metycaine®) hydrochloride with epinephrine are administered above the symphysis pubis and extending over the linear ligament, followed by injections over the posterior distribution of the above nerves in the lumbosacral area. Since this anesthesia suffices only until the cervix is moderately dilated, supplemental methods of anesthesia are required thereafter. Numerous advantages of this type of anesthesia are presented, as well as two contraindications.

The technique of the infiltration procedure as demonstrated is poor. Overemphasis is placed on the safety of this procedure. The photography is good, and the animation is excellent. In its present form this film is recommended only for experienced obstetricians who are capable of evaluating the worth of this procedure and the details of its application.

BUREAU OF LEGAL MEDICINE AND LEGISLATION

MEDICOLEGAL ABSTRACTS

Blood Grouping Tests: Not Admissible as Proof of Paternity.—The state filed a bastardy proceeding against the defendant, charging him with being the father of the child of the complaining witness. The trial court entered a verdict of guilty; so the defendant appealed to the Supreme Court of Ohio.

The statutes of Ohio authorize a trial court, whenever it shall be relevant to the defense in a bastardy proceeding, to order the complainant, her child, and the defendant to submit to one or more blood grouping tests to determine whether the defendant can be excluded as being the father of the child. "In cases where exclusion is established, the results of the tests together with the findings of the expert or experts of the fact of nonpaternity shall be receivable in evidence."

In a prior Ohio case, there was presented the question of proof of nonpaternity in a bastardy proceeding and it was held that the finding and result of a blood grouping test made by a qualified expert from the blood of the complainant, the child, and the person whose nonpaternity was sought to be established was competent for such purpose. In the course of that decision it was also said, "This sort of test is of comparatively recent origin, but medical authorities agree on its accuracy and reliability to establish nonpaternity in the great majority of instances. In the present stage of development, however, it is of no value in proving paternity." Although that statement may be regarded as dicta in that case, said the Supreme Court, it is pertinent in this case, for we are now faced with the specific question of the competency of blood grouping tests to prove paternity. Therefore, it may be here repeated that it is established that there is complete accord of experts in biology on the proposition that results of such blood tests, disclosing a mere possibility of paternity, must be discarded and excluded from evidence as being valueless; and that their admission in evidence is prejudicial.

It cannot be assumed, the court continued, that, in the enactment of the law referred to above, there was any purpose on the part of the general assembly to make competent any such affirmative evidence in such proceedings. By the clear provisions of the code, such blood grouping tests are "required or authorized" only "to determine whether or not the defendant can be excluded as being the father of the child," and it is only "in cases where exclusion is established" that "the results of the tests together with the finding of the expert or experts of the fact of nonpaternity shall be receivable in evidence." Over the strenuous objection of the defendant a concededly qualified pathologist was permitted to testify at length as to the results of a blood grouping test of the complainant, her baby, and the defendant. His findings were so broad and general that they could not properly be applied in the determination of the paternity of complainant's child. Under the limitations prescribed by our statutes the evidence should have been excluded. The resulting prejudice was augmented by the language of the court's charge wherein, following specific reference to the evidence in regard to the blood grouping test, the court stated that it "is not to be concluded by you merely by reason of the fact that blood grouping compared favorably and that this accused could be the father of the child. In other words, the fact alone would not warrant you in finding him the father of this child, that fact alone." That statement, said the Supreme Court, though negative in character, strongly suggested that weight should be accorded such evidence in the determination of the issue submitted. The prejudicial effect of the evidence as thus emphasized by the court's charge becomes clear. Accordingly, the Supreme Court reversed the lower court's findings and remanded the case for further proceedings. Judgment in favor of the state reversed. *State ex rel. Freeman v. Morris, 102 N.E. (2d) 450 (Ohio 1951).*

MEDICAL LITERATURE ABSTRACTS

UNITED STATES

A.M.A. Arch. Dermat. and Syphilol., Chicago

65:639-756 (June) 1952

*Do Roentgen-Ray Treatments as Given by Skin Specialists Produce Cancers or Other Sequelae? Follow-Up Study of Dermatologic Patients Treated with Low-Voltage Roentgen Rays. M. B. Sulzberger, R. L. Baer and A. Borota.—p. 639.
Treatment of Pyodermas with Penicillin 92: Comparison with Neomycin and Bacitracin. H. Rattner and H. H. Rodin.—p. 656.
*Milkers' Nodules: Report of 10 Cases. R. Nomland and A. P. McKee. —p. 663.
Parapsoriasis: Its Treatment with Calciferol: Review of 18 Cases. O. Canizares.—p. 675.
Pityriasis Rubra Pilaris: Clinical and Laboratory Observations on Combined Treatment with Corticotropin and Vitamin A. J. R. Webster and A. B. Falk.—p. 685.
Reticulohistiocytoma of Skin. M. R. Caro and F. E. Senear.—p. 701.
Fallacious Failure Rates in Treatment of Early Syphilis. A. G. Schoch. —p. 714.

Sequelae of Superficial X-Ray Therapy.—In superficial low voltage roentgen ray treatment the practice is to administer to any one area no more than 85 r weekly, up to a maximum total dose of about 1,400 r, measured in air. Dermatologists usually employ from 60 to 100 kv., with half-value layers of about 0.5 to 1 mm. Al, and only in exceptional cases, 120 kv., with half-value layers up to 3 mm. Al. are used. Acne vulgaris, eczema, psoriasis, neurodermatitis, and severe itching are the lesions usually treated by this method. Although dermatologists consider this treatment safe and effective, many physicians believe that the use of superficial roentgen ray treatments is never warranted. The literature does describe sequelae produced by superficial and deep roentgen ray irradiation, but most of the reports deal with cases in which there was no exact information on the type of irradiation. The investigations here reported were undertaken to obtain information on the safety or risks of properly administered roentgen therapy through reexamination of the skins of patients 5 to 23 years later. Of 2,000 patients reexamined, 1,000 had been irradiated and 1,000 were nonirradiated "control" patients. Sequelae were found in 28 patients who had been irradiated, but these were relatively mild and of purely cosmetic significance; there was no ulceration or cancer formation. Ten of these patients had been treated with roentgen irradiation only; the remaining 18 had had other methods of physical and surgical treatment in addition. Twenty-five of these patients had received the roentgen treatments for skin cancers, in which, in order to achieve a cure, one may deliberately administer doses that are expected to produce some roentgen sequelae. Another of these patients had a keloid for which 4,543 r had been administered. The standard doses used currently for treatment of keloid are considerably smaller. There were 211 patients who also had received individual doses of more than 85 r in whom sequelae had not developed. Thus about 1 of every 9 of the 237 patients who received individual single doses of irradiation larger than 85 r had some sort of roentgen sequelae.

Milkers' Nodules.—The term cowpox is confusing because there are two types of cowpox in cows, "natural" cowpox and "genuine" or vaccinia cowpox, caused by two different viruses. Natural cowpox produces milkers' nodules in man, but this virus has not yet been isolated and studied in the laboratory. The virus of vaccinia cowpox, one of the best-studied viruses, rarely causes cowpox in cows except when explosive epidemics occur in herds that have been infected by recently vaccinated persons. Natural cowpox is endemic in herds in Iowa and probably throughout the United States. The earliest lesion in cows is a papule on the teats surrounded by a red areola. The papule rapidly becomes pustular, or a pinhead to pea-sized (1 to 6 mm.) whitish area develops on the surface. The center may be umbilicated or not; the lesion develops a crust. If the crust falls off, there is a granulating ulcer, which heals slowly, producing a slight scar; the complete evolution takes two weeks. The small number of human cases of milkers' nodules compared with the great number of cows having natural cowpox indicates that the disease is not highly contagious to man. The histories of 10 patients with milkers' nodules are discussed. In all instances only one or a few of the cows of a herd had lesions. The vaccination status was recorded in seven patients, five of whom had been successfully vaccinated as children or young adults. Of the two patients not vaccinated, one having active infection with milkers' nodules was successfully vaccinated while he still had a nodule, and the second was vaccinated after the nodule was healed. These facts indicate that vaccination against smallpox does not prevent acquisition of milkers' nodules and that persons with active milkers' nodules can be inoculated with vaccinia. Most of the milkers' nodules started as a small, inflamed area that the patient thought was a simple infection. The lesions enlarged and became nodular, and in two weeks were elevated and firm. One nodule was almost like a verruca; some resembled a granuloma pyogenicum; others contained fluid. There was no widespread eruption. The virus was not isolated; and the authors feel that earlier reports about isolation are equivocal. The virus causing milkers' nodules is not the virus that causes vaccinia, but vaccinia originating from recently vaccinated persons does produce a disease of the teats and udders of cows that is transmissible to human beings, in whom it causes a pock-like eruption rather than nodules.

A.M.A. Arch. Internal Medicine, Chicago

89:859-1000 (June) 1952

Modern Concepts of Acid-Base Regulation. R. F. Pitts.—p. 864.
*Sarcoid-Like Granulomata of Pituitary Gland: Cause of Pituitary Insufficiency. V. R. Bleisch and S. L. Robbins.—p. 877.
Effect of Acute Hypotension on Cerebral Hemodynamics and Metabolism of Elderly Patients. A. N. Bessman, R. W. Alman and J. F. Fazekas. —p. 893.
*Perforation of Interventricular Septum. R. Zucker, S. Leibowitz, H. Brody and R. M. Sussman.—p. 899.
Superiority of Iliac Over Sternal Marrow Aspiration in Recovery of Neoplastic Cells. M. A. Rubinstein and A. Smelin.—p. 909.
Tuberculosis and Sickle-Cell Trait. W. Weiss and W. Stecher.—p. 914.
Morphologic Study of Cardiac Conduction System: VI. Intrinsic Nervous System of Heart. D. J. Glomset and K. R. Cross.—p. 923.
Edema and Hyponatremia. L. G. Welt.—p. 931.
Studies in Mitral Stenosis: III. Effect of Ouabain on Circulation in Patients with Pulmonary Disability. R. A. Bloomfield, B. Rapoport, J. P. Milnor and others.—p. 970.
Canicola Fever: Report of Nine Cases in One Family, with Abstract of World Literature. E. A. Haunz and J. D. Cardy.—p. 978.

Sarcoid-like Granulomas of the Pituitary in Pituitary Insufficiency.—Only 50 cases of pituitary insufficiency resulting from destruction of the pituitary gland by giant cell granulomas have been reported in the literature. The authors screened the records of 14,000 autopsies performed at Boston City Hospital from 1935 to 1950 for examples of granulomatous involvement of the viscera or pituitary. In 12 cases systemic sarcoid-like lesions and pituitaries were available for study. In four cases the lesions were in the pituitary. In one additional case granulomas were limited to the pituitary. In one case the granulomatous lesion showed caseation but there were no demonstrable acid-fast bacilli. Symptoms of pituitary insufficiency were present in one of the patients with disseminated sarcoid-like disease and in the patient with isolated pituitary granulomas. Both

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Titles marked with an asterisk (*) are abstracted.

had severe asthenia, pallor, loss of body hair, and hypochromic anemia; much of the anterior lobe of the pituitary was destroyed. In the two other cases the pituitary lesion apparently produced no symptoms. In one of these cases there were obscure granulomas in the heart and spleen; in the other the granulomatous disease involved the heart and lungs as well as the pituitary. From the study of their own four cases and those collected from the literature, the authors gained the impression that nonspecific granulomatous lesions are found in the pituitary gland with relative frequency in the disease complex of sarcoid and occasionally in tuberculosis. Rarely is the process due to syphilis or trauma. Whether, as Sheehan and Summers believe, there is also a specific pituitary giant cell granulomatous disease cannot be established by the present study.

Perforation of Interventricular Septum.—Perforation of the interventricular septum is an uncommon complication of myocardial infarction. So far 75 cases have been reported, in 28 of which the diagnosis was made during life. Two additional cases of myocardial infarction with rupture of the interventricular septum are reported. The first patient died four and a half years after perforation had occurred, thus representing the second longest recorded survival. The observations on the first patient tend to confirm previous reports of the development of an apical diastolic murmur in the presence of a cardiac aneurysm. In the second patient, the perforation was diagnosed during life and was secondary to infarction caused by atherosclerotic narrowing of an unusual septal branch of the left anterior descending artery. Diagnosis of perforation of the interventricular septum is based on the development of a systolic murmur and thrill, usually most intense in the third and fourth intercostal spaces to the left of the sternum, in a patient with acute myocardial infarction.

A.M.A. Arch. Surgery, Chicago

64:733-850 (June) 1952

*Albumin and Globulin Changes in Burns as Demonstrated by Electrophoresis. J. J. Prendergast, R. L. Fenichel and B. M. Daly.—p. 733.

*Use of Streptokinase-Streptodornase (Varidase®) to Lyse Clotted Blood Obstructing Biliary Drainage: Obstruction Following Cholecystectomy and Choledochotomy. A. St. James, J. F. Connell Jr. and L. M. Rousselot.—p. 741.

Homologous Transplantation of Lung: Preliminary Report of Technical Studies. H. A. Davis, J. P. O'Connor, G. J. Coloviras Jr. and D. L. Strawn.—p. 745.

Posterior Triangle Operations and Trapezius Paralysis. S. Mead.—p. 752.

Partial Gastrectomy With and Without Vagus Resection in Treatment of Duodenal Ulcer: Comparative Analysis of Results of Gastrectomy Alone and Combined with Infradiaphragmatic Vagus Resection. L. T. Palumbo, R. E. Paul and G. T. Westly.—p. 756.

Simple One-Stage Method of Hepatectomy in Dog. J. Markowitz, W. Lotto, J. Archibald and H. G. Downie.—p. 766.

Method of Altering Incidence of Experimental Ulcers in Dragstedt Animals. J. M. Hammer, F. E. Visscher and A. Tazelaar Jr.—p. 773.

Hemangioma of Chest Wall with Extension into Mediastinum and Extradural Space: Report of Case. R. F. Carlson and W. E. Adams.—p. 777.

Influence of Hepatic Artery Ligation on Regeneration of Liver Tissue in Rat. C. E. Wiles Jr., W. G. Schenk Jr. and J. Lindenberg.—p. 783.

Symptoms of Common Duct Stones: Analysis of Clinical Data on 165 Patients Having Explorations of Common Duct. E. L. Strohl, W. G. Diffenbaugh and V. Guynn.—p. 788.

*Defects in Right Diaphragm of Infants and Children with Herniation of Liver. M. M. Ravitch and J. C. Handelsman.—p. 794.

Management of Paroxysmal Hypertension Following Injuries to Cervical and Upper Thoracic Segments of Spinal Cord. E. Bors and J. D. French.—p. 803.

Cutaneous Neurofibromatosis (von Recklinghausen's Disease): Clinical Manifestations and Incidence of Sarcoma in 61 Male Patients. F. W. Preston, W. S. Walsh and T. H. Clarke.—p. 813.

Metabolic Management of Advanced Prostatic Cancer. W. P. Herbst.—p. 828.

Albumin and Globulin Changes in Burns.—Blood protein patterns of eight patients with second and third degree burns involving from 10 to 35% of the total surface area of the body were studied at regular intervals with the Aminco-Stern electrophoresis apparatus from the time of injury until the onset of healing. Results of this first known electrophoretic study of human burn patients indicated that electrophoresis provides a valuable method of evaluating the severity of the burns and the progress of healing. The gamma globulin concentration appeared to provide the best index of burn severity. In relatively minor cases, in which first or second degree burns involved 10 to 15% of the body area, there was little increase in gamma globulin concentration. When second and third degree burns involved 25 to 35% of the body area the gamma globulin concentration was greatly increased. Electrophoretic measurements in this study showed that whole blood transfusions, even when frequently repeated, did not correct the abnormal blood picture produced in moderate to serious burns. Evidence available at this time suggests that purified normal human serum albumin or a blood substitute suitable for albumin replacement should be given to burn patients in addition to whole blood.

Use of a Fibrinolytic Agent in Obstruction of Postoperative Biliary Drainage.—Following cholecystectomy and choledochotomy in a 57-year-old woman with chronic cholecystitis and lithiasis, a T-tube inserted in the common duct drained 150 to 200 cc. of clear bile daily for five days. On the sixth day blood appeared in the T-tube and bile drainage ceased. The patient became icteric, and the serum bilirubin was elevated to 17. The T-tube was threaded with a no. 18 polyethylene® catheter, and a continuous drip (two drops per minute) of isotonic sodium chloride solution containing 400,000 units of streptokinase and 100,000 units of streptodornase per liter was started. At first bloody fluid returned as drainage about the catheter in the T-tube. By the end of 96 hours the return fluid contained clear bile. This was associated with a lessening of the icterus, a fall in the serum bilirubin, and a sense of well-being on the part of the patient. Continuous perfusion of the obstructed lumen of the common bile duct with streptokinase and streptodornase (varidase®) resulted in the nontraumatic removal of the clotted blood from the obstructed external biliary drainage system, thereby obviating a major surgical procedure in a critically ill patient. The same method also was used to relieve acute urinary retention secondary to blood clots in the bladder following suprapubic prostatectomy. When enzymes are used in such conditions, the physiological criteria peculiar to each enzyme system, such as pH, specific substrates available, and concentration of active enzyme must be met and maintained.

Protrusion of Liver Through Diaphragmatic Defects.—Attenuation of the central section of the right side of the diaphragm, which is normally muscular, is reported in five children. The defect was circular, well defined, and ringed by normal diaphragmatic muscle. Its diameter varied from 4 cm. to half that of the right diaphragm. The smaller lesions resembled a true diaphragmatic hernia in that the surrounding normal phrenic muscle acted as a ring and the thinned-out membrane encompassed by it bulged into the thorax under abdominal pressure, as does a hernia sac. Protrusion of the liver through the defect produced respiratory embarrassment or liver necrosis. Troublesome coughs in two of the authors' patients disappeared after surgical repair of the diaphragm. Episodes of apnea and cyanosis in a third patient gradually subsided postoperatively, but the subsequent development of symptoms suggestive of a congenital cerebral defect or injury made it difficult to evaluate the role of the diaphragmatic abnormality. An incision through the fourth or fifth interspace anterolaterally or in the eighth interspace posterolaterally offered ample exposure. The "sac" overlying the liver was opened, and the incision was carried through the phrenic ring, if necessary. Reduction of the liver was accomplished without difficulty. The excess attenuated membrane was inverted, and the defect was plicated in the direction of the incision. In one case biopsy of the "sac" revealed fibrous tissue microscopically indistinguishable from the tendinous portion of the diaphragm. In three other cases "muscle" or "scarred muscle" was found, thus differentiating this lesion from a true hernia sac and suggesting that the underlying pathological condition may be a localized affection of diaphragmatic innervation. Convalescence from the surgical procedure was uneventful in all five patients. Clinically and roentgenologically the correction in each case was complete and maintained. Surgical correction is the recommended treatment in all cases of this type, for the same reason that it is indicated in the usual cases of diaphragmatic hernia. The described abnormality should be considered in the differential diagnosis of masses low in the right chest that are roentgenologically sharply demarcated superiorly and not separable from the diaphragm inferiorly.

Alabama State Medical Assn. Journal, Montgomery

21:353-404 (June) 1952

Management of Viral Hepatitis. J. A. Davis Jr.—p. 353.
Congenital Atresia of Nasal Choanae. G. E. Johnson.—p. 357.
Intramedullary Fixation of Fractures. J. S. DuBois.—p. 361.

American Heart Journal, St. Louis

43:801-962 (June) 1952

Effect of Changes in Concentration of Cations on Electrocardiogram of Isolated Perfused Heart. W. A. Butcher, K. G. Wakim, H. E. Essex and others.—p. 801.
Relationship Between Electrocardiographic Changes and Hypokalemia in Insulin-Induced Hypoglycemia. A. E. Parrish, S. J. N. Sugar and J. F. Fazekas.—p. 815.
*Case of Spontaneous Thrombosis of Superior Vena Cava with some Observations on Mechanism of Edema Formation. L. Rice, J. Frieden, L. N. Katz and others.—p. 821.
A-V Conduction Disturbance in Presence of Pre-Excitation Syndrome. D. Scherf, S. Blumenfeld and P. Mueller.—p. 829.
Identification of Complexes of Electromagnetic Ballistocardiogram in a Single Channel. N. S. Blackman.—p. 840.
Study of Volume-Time Course of Pulse Wave of Finger Tip. G. E. Burch, C. T. Ray and G. S. Berenson.—p. 844.
*Experimental and Clinical Study on Effects of Procaine Amide (Pronestyl) on the Heart. J. Zapata-Díaz, E. Cabrera and R. Méndez.—p. 854.
*Evaluation of Anticoagulant Therapy in Treatment of Acute Myocardial Infarction. H. I. Russek and B. L. Zohman.—p. 871.
Quantitative Stethoscope and Its Clinical Applications. E. Lepeschkin.—p. 881.
Gangrene Resulting from Thromboarteritis, Apparently of Rheumatic Fever Origin, with Special Reference to Histopathology of Rheumatic Aortitis and Arteritis and Occurrence of Thrombosis. K. Y. Ch'in, M. Y. Tang and F. S. Liu.—p. 889.
Interventricular Septal Defect Complicated by Pregnancy. W. C. Swann.—p. 900.
Subacute Bacterial Endocarditis Complicated by Intermittent Complete Heart Block and Stokes-Adams Attacks. W. Whitaker.—p. 904.
Pronestyl (Procaine Amide) Therapy in Paroxysmal Ventricular Tachycardia. E. Antzis, J. J. Dunn and A. J. Schilero.—p. 911.
Tetralogy of Fallot with Subacute Bacterial Endocarditis: Successful Treatment with Chloromycetin. M. Spring and H. Wardell.—p. 918.
Combined Use of Aureomycin and Terramycin in Treatment of Subacute Enterococcal Endocarditis. E. Rubenstein and P. G. M. Austin.—p. 922.

Thrombosis of Superior Vena Cava and Edema Formation.—It has been assumed that localized edema and edema consequent to obstruction of the superior vena cava results solely from the local increase in venous and capillary hydrostatic pressures. However, recent work has shown that edema associated with venous congestion is accompanied by alterations in renal function. For example, experiments in dogs suggested that peripheral venous pressure elevation following constriction of major veins leads to an increase in renal tubular sodium reabsorption, which tends to parallel the extent of venous congestion. As venous congestion declines through the development of collateral channels, renal sodium excretion returns to normal. The authors present the case of a man, aged 50, with apparently spontaneous thrombosis of the superior vena cava. This patient's ability to excrete salt ingested orally was impaired in comparison to that of healthy persons. The authors present evidence that the edema formation of the superior vena cava syndrome is due to an abnormal increase in tubular reabsorption of sodium, which parallels the degree of venous congestion.

Effects of Procaine Amide (Pronestyl®) on Heart.—Most investigators agree that procaine amide (pronestyl®) is more effective in ventricular than in auricular arrhythmia. Zapata-Díaz and associates describe their experiences with this drug in two groups of dogs and in 37 patients. Fifteen of the patients had auricular extrasystoles and paroxysmal auricular tachycardia; six had paroxysmal auricular fibrillation and auricular flutter; eight had ventricular extrasystoles; and eight had paroxysmal ventricular tachycardia. From their observations the authors conclude that procaine amide increases the threshold of excitability and slows down the speed of conduction both in the auricles and in the ventricles. It has little effect on the auriculoventricular conduction when the heart maintains sinus rhythm. The impairment of atrioventricular and intraventricular conduction is greater when the rate of the pacemaker is higher. Equal doses have a greater effect on intraventricular conduction when administered in a single intravenous injection than by slow venoclysis. Procaine amide is effective in auricular disorders. It relieves auricular extrasystoles and supraventricular paroxysmal tachycardia, and it can slow down the rate of auricular fibrillation or flutter. Since paroxysmal auricular tachycardia responds favorably to acetylcholine or its derivatives, procaine amide should be used in cases in which acetylcholine is ineffective or contraindicated. Procaine amide should be the drug of choice in ventricular arrhythmias (extrasystoles, ventricular flutter, and paroxysmal ventricular tachycardia). It should be administered orally or intravenously according to the severity of the case. In auricular flutter, the use of procaine amide is dangerous, because it can lead to a 1:1 atrioventricular response, with aberrant intraventricular conduction, eventually inducing ventricular flutter or fibrillation. In paroxysmal auricular fibrillation, procaine amide may reestablish a sinus rhythm but its use is not without danger. In arrhythmias due to overdosage of digitalis or its derivatives, procaine amide can clear up ventricular extrasystoles produced by digitalis, but its improper use can favor the occurrence of ventricular flutter or ventricular fibrillation. This danger may be reduced by giving procaine amide by slow venoclysis.

Anticoagulant Therapy in Acute Myocardial Infarction.—An analysis was made by Russek and Zohman of 1,047 consecutive patients admitted for acute myocardial infarction, all of whom were treated without anticoagulants. The over-all mortality rate was 33.4%, but in the good risk group it was only 3.1% as compared to 60.0% in the poor risk group. In investigating the possible benefit of anticoagulants in 489 good risk patients, the authors gained the impression that no more than one death among every hundred patients could have been prevented by bishydroxycoumarin. Moreover, the drug could have averted only eight clinical thromboembolic episodes in 1,000 patients, since this was the incidence of this complication in the good risk group. Such theoretical benefit is unimpressive when compared with the risks inherent in interference with blood clotting. To determine current opinions concerning the use of anticoagulant drugs in acute myocardial infarction, a questionnaire was forwarded to internists and cardiologists in medical centers throughout the United States. More than one-half of the 228 physicians who replied do not employ anticoagulants as a routine measure in acute myocardial infarction. Many are guided by the history and the severity of the clinical symptoms. Five physicians do not use anticoagulants at all, because they doubt that the value outweighs the potential hazards. The 111 physicians advocating selection of cases enumerated the following indications for anticoagulant therapy: previous myocardial infarction, the presence of a large infarct, profound or persistent shock, intractable pain, significant enlargement of the heart, cardiac arrhythmias, thromboembolic phenomena, varicosities, previous or recent thrombophlebitis or phlebothrombosis, old age, debility, lethargy, obesity, diabetes, polycythemia, and any departure from a smooth or uneventful course. A total of 112 of 228 physicians reported that they routinely employ anticoagulants in acute myocardial infarction when no contraindications exist. Some emphasized that they were forced to follow this practice, because failure to use these drugs "is often construed by the family, referring physician, and consultant as mistreatment." Hospitalization and dependable laboratory facilities are an absolute necessity when anticoagulants are to be employed in myocardial infarction. Most physicians either use bishydroxycoumarin (dicumarol®) alone or in combination with heparin. Heparin is usually reserved for serious cases. Ethyl biscoumacetate (tromexan®) ethyl acetate is used alone or in conjunction with bishydroxycoumarin and/or heparin by a smaller but significant number of physicians. Hemorrhagic complications resulting from anticoagulant therapy caused 122 fatalities, according to the reports of 64 physicians. The incidence of serious hemorrhage following anticoagulant therapy varied between 0.25% and 10% and of resulting fatalities up to 4%. The authors conclude that routine employment of anticoagulant therapy in acute myocardial infarction is neither necessary nor desirable.

American Journal of Clinical Pathology, Baltimore

22:509-604 (June) 1952. **Partial Index**

Pathologic Findings in Patients Dead of Common Poisons. L. Adelson. —p. 509.
Unusual Histiocytic Reaction to Lymph Nodes in Letterer-Siwe Disease. N. G. B. McLetchie.—p. 520.
Mycotic Brain Abscess Due to Cladosporium Trichoides, New Species: Report of Case. C. H. Binford, R. K. Thompson and M. E. Gorham. —p. 535.
Capillary-Tube Method of Rhesus Testing, with Report on Blood Group Frequencies in North West London. G. Discombe and H. Meyer. —p. 543.
Bacteriologic Studies in Epidemic of Bacillary Dysentery in Korea: Serotypes of Shigella and Salmonella Recovered and Bacteriologic Response to Sulfadiazine, Chloramphenicol, Terramycin, Aureomycin and Streptomycin. L. E. Zimmerman, M. Cooper and C. D. Graber.—p. 549.
Cytology in Bronchiogenic Carcinoma. W. Umiker.—p. 558.

American Journal of Medical Sciences, Philadelphia

223:589-708 (June) 1952

Geriatrics: Past, Present and Future. O. H. P. Pepper.—p. 589.
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*Rheumatic Fever During First Few Years of Life and Its Differentiation From Endocardial Fibrosis. R. B. Logue and J. W. Hurst.—p. 648.
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Ventricular Rate Response Following Exercise During Auricular Fibrillation and After Conversion to Normal Sinus Rhythm. D. G. Wetherbee, M. G. Brown and D. Holzman.—p. 667.
Hypertension in Children: Review. W. W. McCrory and F. W. Nash. —p. 671.
Diabetes Mellitus and Pregnancy with Special Reference to Fetal and Infantile Loss. C. Bachman.—p. 681.

Red Cell Mass in Rheumatoid Disease.—Thirty patients with rheumatoid disease associated with anemia of the normocytic or microcytic, hypochromic variety were treated with red cell mass transfusions. Transfusions were given in courses of 4, 6, or 10 units. Each transfusion consisted of 1 unit of red cell mass, i. e., the sedimented cells of 1 pt. (500 cc.) of whole blood after the plasma is withdrawn. Mild transfusion reactions were noted in only two patients. Follow-up of patients varied from three months to three years. All patients showed improvement in the levels of hemoglobin, sedimentation rate, hematocrit, and blood volume. Comparison of whole blood volume and plasma volume in 25 patients with rheumatoid arthritis and in 25 normal persons revealed a greater plasma volume in persons with rheumatoid disease. This appears to be the mechanism of the anemia. Before transfusion, plasma volume ranged from 53 to 62% of the total blood volume. Within one week of the red cell mass transfusions, it ranged between 32 and 44%. Clinical improvement was seen in every patient receiving red cell mass transfusions; pain and stiffness became minimal, appetite improved, the range of motion of joints was increased, and swelling, tenderness, nodules, and muscle spasm decreased. Of five patients who relapsed, one required three courses of red cell mass transfusion over a period of four months, but has remained in remission for the past year. Transfusions of red cells restore the normal cell plasma relationship and should be employed with greater frequency in the management of the rheumatoid patient. A course of 6 to 10 units, given as 1 unit daily, will produce the most beneficial results; such courses may be repeated as required.

Rheumatic Fever During First Five Years of Life.—In 26 patients less than 5 years old with rheumatic fever the suspected age of onset was 5 years in 6, 4 years in 9, 3 years in 3, 2 years in 5, 1 year in 2, and unknown in 1. The diagnosis was established by necropsy in four patients and by the presence of characteristic features of rheumatic infection or the development of rheumatic heart disease after a long term follow-up in the remaining cases. The predominant manifestations were myocarditis or valvular lesions. Significant systolic murmurs at the apex were present in 22 patients. Joint symptoms occurred in 14 patients, but objective signs were present in only 9. The predominantly apical location of murmurs due to rheumatic disease as contrasted to the predominantly midsternal and basal location of murmurs in congenital disease should differentiate the two. Endocardial fibrosis rather than rheumatic fever is suggested if no murmurs are heard in the presence of congestive heart failure. A long-time survival after the onset of congestive heart failure favors rheumatic infection, since the majority of patients with endocardial fibrosis die within a year after heart failure ensues. The presence of pericarditis rules out endocardial fibrosis and offers strong corroborative evidence of rheumatic fever. The development of aortic insufficiency later during the course of the disease favors rheumatic fever. The presence of coarctation with a large heart and congestive failure suggests endocardial fibrosis. The authors' experience with the 26 cases of rheumatic fever occurring at the age of 5 or less suggests that the disease is commoner in this group than has been previously suspected.

American Journal of Public Health, New York

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Industrial Noise: Its Effect and Control. C. I. Barron and F. E. Poole. —p. 705.
Value of Influenza Virus Vaccination in Industry. C. F. Yeager.—p. 723.

Conjunctivitis Due to Newcastle Disease Virus.—Among 90 workers on an eviscerating line in a chicken cannery 40 had conjunctivitis. Symptoms consisted of irritation of the involved eye, lacrimation, redness, and some swelling of the conjunctiva, but no involvement of the cornea. Edema of the lids was present in varying degree. Photophobia or visual impairment was uncommon. Preauricular adenitis on the affected side was present in about half the cases. No constitutional symptoms were noted, and headache was uncommon. Usually only one eye was involved. A review of the company records for 1950 showed that 10 cases of conjunctivitis were reported during that year. These also were limited to workers on the eviscerating line. Two of the 1950 patients had recurrent attacks and one of them also had conjunctivitis in 1951. The isolation of the virus of Newcastle disease from 4 out of 10 cases seems to establish this as the etiological agent in the outbreak.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

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Am. Practitioner & Digest of Treatment, Philadelphia

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Permanence of Effects of Modern Chemotherapeutic and Antibiotic Agents in Urinary Tract Infections, with Special Reference to Terramycin in Resistant Conditions. J. A. Lazarus and W. A. Wood.—p. 445.
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The General Practitioner's Obligation to Industrial Medicine. E. Matlin. —p. 460.
Ballistocardiography: Historical Review and Clinical Observation. J. E. Doherty.—p. 464.
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Cryptococcic (Torula) Meningo-Encephalitis. W. H. Stimson and K. F. Dean.—p. 476.
Glucose Tolerance: III. Evaluation of Four Types of Tests in Heterogenous Group of 71 Subjects with Glycosuria. C. R. Womack and J. H. Moyer Jr.—p. 479.

Annals of Internal Medicine, Lancaster, Pa.

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Ménière's Disease: Its Pathologic Features, Clinical Expressions and Therapy. M. Saltzman.—p. 1157.
Ménière's Syndrome as Premonitory Symptom of Cerebrospinal Vascular Occlusion: Report of Two Cases. W. G. Ensign.—p. 1167.
Treatment of Angina Pectoris with Khellin: Part I. J. J. Conn, R. W. Kissane, R. A. Koons and T. E. Clark.—p. 1173.
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*Pulmonary Infiltration with Eosinophilia (PIE Syndrome). W. H. Reeder and B. E. Goodrich.—p. 1217.
*Cholangiolitic Biliary Cirrhosis (Primary Biliary Cirrhosis). W. E. Ricketts and R. W. Wissler.—p. 1241.
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Analysis of the Phenomenon of "Anticipation" in Diabetes Mellitus. A. G. Steinberg and R. M. Wilder.—p. 1285.
Prolonged Renal Salt Wastage in "Lower Nephron Nephrosis." R. B. Hunter and E. E. Muirhead.—p. 1297.

Syndrome of Pulmonary Infiltration with Eosinophilia.—The similarities between Loeffler's syndrome, tropical eosinophilia, and other diseases of suspected allergic origin in which pulmonary infiltration and blood eosinophilia coexist suggest that these conditions be grouped under a common designation. Pulmonary infiltration with eosinophilia (PIE syndrome) has descriptive appeal and, when accompanied by a subsidiary or modifying diagnosis, affords a clear image. An example of such a diagnosis would be a diagnosis of the PIE syndrome associated with bronchial asthma. The authors observed eight patients with the PIE syndrome and various accompanying conditions in 18 months. Four illustrative cases are described in detail. In the first of these patients symptoms and physical and radiographic findings were initially suggestive of viral pneumonitis, for which antibiotics were given. Later, when eosinophilia and the PIE syndrome were recognized, the patient responded to cortisone. In the second patient corticotropin (ACTH) was effective, although spontaneous remission cannot be definitely ruled out. In the third patient severer illness, albuminuria, urinary casts, hematuria, and altered plasma proteins, with a progressive downward course prior to treatment, suggested a severer process than existed in cases 1 and 2. Periarteritis nodosa could not be excluded. The pathological processes seemed to be interrupted during treatment with corticotropin. In the fourth patient, progressive periarteritis nodosa accompanied the PIE syndrome. Pulmonary infiltration present prior to cortisone therapy had cleared before the patient died following a cerebrovascular accident. Periarterial eosinophilic infiltration was substantially less in autopsy sections than in biopsy specimen prior to therapy. The cases illustrate that disorders of variable severity may accompany the PIE syndrome.

Cholangiolitic Biliary Cirrhosis.—Ricketts and Wissler point out that among the various forms of biliary cirrhosis a clinicopathological entity can be segregated in which the main lesion consists of an inflammation in and around the smaller bile ducts (Hering's canals or junction ducts), or in the canaliculi between the lobules, or both. The term cholangioles as used here includes both the finer biliary radicles and the bile canaliculi, and the term cholangiolitic cirrhosis is applied to the inflammation of these areas. Other synonyms for this disorder are pericholangiolitic biliary cirrhosis, chronic intrahepatic obliterating cholangitis, nonobstructve cholangitic biliary cirrhosis, intrahepatic cholangitic biliary cirrhosis, Hanot's biliary cirrhosis, and cholangitis lenta. Since there is much controversy about this form of biliary cirrhosis, the authors describe observations on nine cases. They differentiate two clinical forms of cholangiolitic cirrhosis, one with and one without xanthomatosis. In two women with xanthomatous biliary cirrhosis, chronic jaundice, hepatomegaly, splenomegaly, xanthomatosis, and pruritus were the most conspicuous clinical features. Edema, ascites, and collateral abdominal circulation were absent. There was no significant loss of weight or pain in the right upper quadrant. Three males and four females with nonxanthomatous biliary cirrhosis from 10 to 64 years of age had fever, jaundice, loss of weight, and pruritus. Hepatomegaly was observed initially in six cases; in the seventh the liver later became hard and firm. Splenomegaly was evident clinically in five cases, and in another enlargement of the spleen was found at laparotomy. Jaundice varied in degree but was chronic. There were similar biochemical deviations in both forms of cholangiolitic cirrhosis. Evidence of bile regurgitation was present. The results of tests based upon the altered colloid stability of the serum, such as thymol and cephalin cholesterol flocculation, were abnormal. Electrophoretic separation of the serum proteins disclosed in both types of cases the peak elevation of the beta globulin fraction characteristic of biliary cirrhosis. The enlarged liver had a smooth or slightly nodular surface without the hobnail appearance. The liver parenchyma was preserved and there were no fatty, degenerative, or diffuse necrobiotic features. The above observations supply no additional information about the pathogenesis, but there is no evidence that it is a parenchymatous liver disease.

Diabetes, New York

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Relation of Glutathione to Diabetogenic Effect of Adrenal Steroids. A. Lazarow.—p. 171.
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Acetone in the Breath: Study of Acetone Exhalation in Diabetic and Nondiabetic Human Subjects. M. J. Henderson, B. A. Karger and G. A. Wrenshall.—p. 188.
*Evaluation of Method of Self-Testing for Diabetes: Report of the Gloucester Diabetes Study. V. A. Getting, H. F. Root, H. L. C. Wilkerson and others.—p. 194.
Temporary Insulin Resistance: Report of Case Requiring 5490 Units of Insulin in 24 Hours. J. H. Crampton and C. D. Davis.—p. 201.
*Mortality from Diabetes Throughout the World: Characteristics and Trends. L. I. Dublin and H. H. Marks.—p. 205.

Self-Testing for Diabetes.—A study was made by the Massachusetts Department of Public Health, the diabetes control section of the United States Public Health Service, and the diabetes committee of the Massachusetts Medical Society in Gloucester

to ascertain the community's ability to perform a specific procedure, i. e., the self-test for urine sugar, in a diabetes mellitus detection program. The town has a population of approximately 28,000 persons. With the cooperation of the Gloucester drugstores, self-testing kits were made available for public distribution free of charge. Each kit contained sufficient material to perform two urine tests, and included printed instructions for the collecting and testing of specimens, with advice to report any "suspicious" findings to a physician. Each person had to go to a drugstore and register by name, address, and date in order to obtain the kit, thus enabling the interviewing team to contact participants for follow-up studies regarding the use of the test material. With adequate community organization providing advance publicity, good acceptance of the program by the public was obtained. An analysis of follow-up studies on 2,911 persons who had obtained self-test kits revealed that 1,730 (59%) actually performed the self-test and 1,181 (41%) failed to use the equipment. The majority of those who did not test their urine either lost interest in the project or procrastinated in carrying out the procedure. More fear of the disease was observed among those who performed the test, which was associated with close contact with diabetes mellitus in the family, among friends, or in the spouse's family. Of the 1,730 persons who performed self-tests, 1,526 (88%) had negative results, 98 (5.6%) had positive results, and 106 (6.2%) had undetermined results (single green color changes). Only 23 (23.5%) of the 98 persons with positive results interpreted these findings as indicating a need for medical advice and visited their physicians for diagnostic follow-up studies, while 34 (34.7%) of the positive group believed that their tests indicated that they had no disease or no sugar in their blood or urine. Thus 75 (76%) of the 98 persons with positive results failed to obtain medical advice. The implication of such results make clear that a great increase in efforts to disseminate health information to the public is needed. To obtain a high degree of performance of even as simple a test as that for glycosuria, maximal cooperation, including participation of all physicians as well as all public health agencies, is desirable.

Mortality from Diabetes.—The classification procedure inaugurated with the sixth revision of the International Lists of Diseases and Causes of Death has brought a sharp reduction in the recorded mortality from diabetes mellitus in the United States and many other countries. This procedure came into use in 1949 in some areas and in 1950 in others, and, except as noted, the authors' statistics relate to the classification by the fifth revision. The long-term trend of diabetes mortality in the United States has been upward, but a major part of this rise has been due to aging of the population. The age-adjusted death rate actually decline from 1940 to 1948. At the childhood and early adult ages death rates from diabetes mellitus have steadily fallen in the United States since insulin came into use. The rates at older ages showed a pronounced increase, particularly among women, until about 1940, but have declined considerably since then. Trends of the rates by states and in the large cities of the country between 1938 and 1948 showed pronounced variation. Death rates from the disease by states are generally lowest in the South and Southwest and highest in the North. The death rates from diabetes mellitus in the various countries of the world have a relatively wide range. The rate is highest in the United States and in some other English-speaking countries with an abundance of food, so that in part at least their death rates reflect high living standards and high food intake. At the same time the search for diabetes mellitus had probably been most intensive in these countries, partly because of their abundant medical resources and the increased use of laboratory tests in clinical and hospital practice. The death rates are much lower in eastern and southern Europe, Central and South America, and Asia, and lowest of all in the undeveloped countries. The variation in rates is due in part to differing practices in medical certification of causes of death and in evaluation of the facts reported. The true situation is not known. Postwar rates in Europe are generally much lower than prewar rates. There is ground for the belief that the trend of diabetes mortality there affords a practical demonstration of control of diabetes mellitus on a large scale by enforced dietary restriction. The statistics by sex and age, presented for a number of countries, showed almost uniformly a higher mortality in female patients than in males, and without exception a rise in mortality with age. The death rates during 1949-1951 in the United States, based on the sixth revision, have been fairly stable for the country as a whole, with 16.5 per 100,000 in both 1949 and 1951 and 16.6 in 1950. The effect of the revised procedure varies by age, race, and religion, but is greatest in the middle and later age groups in which diabetes mellitus is most prevalent.

Endocrinology, Springfield, Ill.

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Organic and Inorganic Iodine Levels in Serum of Sheep Receiving Daily Oral Doses of I^{131}. M. H. Weeks, J. Katz and N. G. Farnham.—p 511.
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Adrenal Ascorbic Acid Changes in Gonadectomized Golden Hamster Following Single Injection of Diethylstilbestrol. B. C. Wexler.—p. 531.
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Physiological Interaction of Cortisone Acetate and Diethylstilbestrol. Lack of Androgenic or Estrogenic Effects of Cortisone Acetate. P. Talalay, M. M. Dobson, C .M. Ebersole and C. Huggins.—p. 574.

Geriatrics, Minneapolis

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SYMPOSIUM ON GERIATRIC SURGERY

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Geriatric Significance of Skin Diseases Due to Waterproof Footwear. L. E. Gaul and G. B. Underwood.—p. 198.
Leonardo da Vinci's Studies of the Aging Process. E. Belt.—p. 205.

Hawaii Medical Journal, Honolulu

11:279-318 (May-June) 1952

*Recent Improvements in Surgical Treatment of Low Back Pain Due to Ruptured Lumbar Intervertebral Disks. R. B. Cloward.—p. 279.
Conduct of Premature Labor. H. E. Bowles.—p. 286.
Treatment of Viral Enteritis with Vitamin B Complex. D. H. Murray. —p. 289
Sclerosing Lipogranuloma: Case Report. D. H. Bell and W. H. Civin. —p. 291.

Improved Surgical Treatment of Ruptured Intervertebral Disks.—After trying various surgical procedures in the treatment of ruptured intervertebral disks, Cloward developed a new method involving fusion of the vertebral bodies. His aim was to preserve or to reestablish the normal intervertebral space and to stabilize the weak joint by fusion of the adjacent vertebral bodies. To accomplish this an effort was made to remove the intervertebral disk, including the cartilaginous plate and cortical surface of the vertebral bodies, and to replace it with plugs of bone. The bone plugs are full thickness grafts obtained from the crest of the ilium. This procedure had been employed by Cloward since 1944 in a total of 250 patients. The high percentage of permanent cures with no residual disability compared to those treated before 1944 convinced him that this operation is the treatment of choice for ruptured lumbar intervertebral disk. Patients can be discharged from the hospital in about 10 days, and the use of a Taylor back brace is unnecessary. The shortening and fibrosis of the muscles that may result from wearing a brace too long is avoided. The author describes several new instruments that he found helpful for vertebral body fusion, including a self-retaining spinal dura retractor, a vertebra spreader, and specially designed blades for the self-retaining laminectomy retractor. During the first three years this opera-

tion was carried out, the average time required was over four hours, since bone had to be removed from the crest of the ilium. Furthermore, after the operation patients often complained most of pain over the ilium, and this pain sometimes continued for months or years. To prevent this hip pain and to shorten the operation, Cloward has used preserved bone from a bone bank for the grafts in a total of 87 vertebral body fusions. The author emphasizes that his fusion operation has reduced the period of disability following the operation and has lessened considerably the expense of the illness both in time off from work and in cost of hospitalization.

Illinois Medical Journal, Chicago

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American Medicine on the March. C. P. White.—p. 289.
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Typhus Fever. H. N. Kamin, H. S. Lakin, G. L. Schaefer and M. Goldin. —p. 320.
Carcinoma of Thyroid in Children. R. H. Lawler, J. W. West and E. G. Lawler.—p. 322.

Indiana State Medical Assn. Journal, Indianapolis

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Journal of Allergy, St. Louis

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*Death Occurring in Bronchial Asthma: Report of Five Cases. I. Walzer and T. T. Frost.—p. 204.
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Inhalation Test as Diagnostic Procedure with Special Emphasis on House Dust Allergen. I. W. Schiller and F. C. Lowell.—p. 234.
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Time of Day of Pollen Shedding of Some Hay Fever Plants. M. D. Jones.—p. 247.
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Contribution to Study of Reticulo Endothelial Origin of Dust Cells or Alveolar Macrophagi: VI. Histochemical Aspects in Lungs of Normal Guinea Pigs and Others Submitted to Acetylcholine, Histamine, or Anaphylactic Shock, and So-Called Experimental Asthma. E. A. Pedace, A. E. Bachmann and G. Ruiz-Moreno.—p. 265.
Bronchial Asthma Due to Rat and Mouse Hair: Report of Two Cases. F. H. Chafee.—p. 277.

Death in Bronchial Asthma.—Analysis of five cases in which death occurred as the result of an asthmatic paroxysm shows that intrinsic asthma, unlike common allergic asthma, is a definite threat to life. Hyalinization of the basement membrane, hypertrophy of the bronchial musculature, hyperactivity of the bronchial mucous glands, and plugs of thick mucus in the bronchi are the typical findings on postmortem examination; emphysema almost always occurs in fatal cases. The actual cause of death in patients dying in an asthmatic paroxysm seems to be obstruction of the bronchial tree by mucus that has become extremely viscid, thick, and tenacious as the result of some unknown process. Bronchodilating drugs, such as aminophylline and ephedrine, given at intervals throughout the day and night have proved useful in affording protection against acute obstructive attacks. The dosage should be adjusted to the patient's need and tolerance for the drug. Potassium iodide is also given two or three times a day in doses large enough to insure a liquid sputum. This method of treatment has been in use for the last two years at the Veterans Administration Center at Whipple, Ariz. During that time only one patient has died in an asthmatic paroxysm, although a large percentage of the patients at the center have been sent to Arizona because of severe, intractable pulmonary disease.

Journal-Lancet, Minneapolis

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Education for Childbirth in Private Practice: Report on 585 Consecutive Cases. H. L. Miller and F. E. Flannery.—p. 274.
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Surgical Treatment of Recurrent Carcinoma of Cervix. W. C. Keettel, E. S. Brintnall and J. H. Randall.—p. 283.
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Menstrual Variations Associated with Changes in Altitude S. H. Sikkema.—p. 288.
Ectopic Pregnancy and Attempted Criminal Abortion: Report of Case. J. C. Doyle.—p. 294.
Endometriosis. F. J. Hofmeister and L. R. Grinney.—p. 296.

Journal Nat. Cancer Inst., Washington, D. C.

12:937-1158 (April) 1952. **Partial Index**

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Tumors of Glandular Stomach Induced in Rats by Intramural Injection of 20-Methylcholanthrene. W. V. Hare, H. L. Stewart, J. G. Bennett and E. Lorenz.—p. 1019.
Production of Sarcomas from Cultured Tissues of Hepatoma, Melanoma, and Thyroid Tumors. K. K. Sanford, G. D. Likely, V. J. Evans and others.—p. 1057.
Growth and Histopathology of Melanotic and Amelanotic Derivatives of Cloudman Melanoma S91. P. Loustalot, G. H. Algire, F. Y. Legallais and B. F. Anderson.—p. 1079.
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Transfer of Mammary Tumor Milk Agent from Implant to Host. R. T. Prehn.—p. 1127.
Interrelation of Specific Genes, Body Weight, and Development of Tumors in Mice. W. E. Heston, M. K. Deringer, I. R. Hughes and J. Cornfield.—p. 1141.

Journal of School Health, Buffalo, N. Y.

22:155-188 (June) 1952. **Partial Index**

Teammates—Teachers and School Nurses. G. E. Cromwell.—p. 165.
*Vision Problems of School Children. G. L. Witter.—p. 179.

Vision Problems of School Children.—Visual testing of school children has three objects: (1) to assure educators that the eyes of the child are adequate for school life; (2) to prevent progress of pathological conditions by early recognition and treatment; and (3) to help the visually handicapped by correcting refractive errors by means of glasses. The schools with which Witter is concerned use as equipment "The Massachusetts Vision Test," which is simple, brief, economical, and provides detection of latent errors in binocularity, latent errors in refraction, and reduced visual acuity. Every year the school nurse tests all first and sixth grade students. By examining the first graders early in the school year, many with visual handicaps are found and the parents notified. Bodily growth and development between the ages of 6 and 11 are rapid, and many refractive errors develop and some latent defects in ocular motility become evident. It is therefore advisable that sixth grade students be retested before they begin the more intense academic years of junior high school. The records of those first grade students found to have visual defects are filed separately, and these children are rechecked yearly to be sure that their eye condition is corrected. Proper care for the eyes of school children requires the cooperation of teachers, school nurses, parents, and the family's oculist.

Journal of the Student A.M.A., Chicago

1:1-72 (June) 1952

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Medical Indications for Splenectomy. L. R. Limarzi.—p. 31.

Maryland State Medical Journal, Baltimore

1:215-266 (May) 1952

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Minnesota Medicine, St. Paul

35:381-500 (May) 1952

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Childhood Mortality from Accidents. A. B. Rosenfield.—p. 424.
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Surgery, Gynecology and Obstetrics, Chicago

94:641-766 (June) 1952

Note on Estimates of Rate of Development of Metastasis in Patients with Cancer of Breast. A. G. Gilliam.—p. 641.
*Cancer of Breast: Analysis of Frequency, Distribution, and Mortality at the University of California Hospital, 1918 to 1947, Inclusive. M. B. Shimkin, E. L. Lucia, R. S. Stone and H. G. Bell.—p. 645.
*Antibacterial Substance in Human Semen and Prostatic Fluid. P. W. Taylor and H. R. Morgan.—p. 662.
Variations in Formation and Vascular Relationships of Bile Ducts. E. V. Johnston and B. J. Anson.—p. 669.
Closed Gravity Technique for Preservation of Whole Blood in ACD Solution Utilizing Plastic Equipment. C. W. Walter and W. P. Murphy Jr.—p. 687.
Bedside Urological X-Ray Examination of the Severely Injured Patient. L. A. Orkin.—p. 693.
Observations on Use of Artificially Induced Progestational State as Preoperative Adjunct to Radical Pelvic Surgery. J. K. Cromer, R. Hertz and J. P. Young.—p. 703.
Urologic Procedures Employed in Diagnosis of Urinary-Vaginal Fistulas. J. R. Longley and L. F. Greene.—p. 709.
Changes in Blood Volume Following Administration of Dextran—Determined by P^{32} Labeled Red Cells. L. M. Meyer, N. I. Berlin, G. M. Hyde and others.—p. 712.
Role of Radiation and of Surgery in Management of Uterine Carcinoma. F. L. Payne.—p. 715.
Physiologic Resection of Right Colon. J. P. Barnes.—p. 722.
Intramedullary Nailing in Presence of Infection: Experimental Study in Dogs. H. L. Rush Jr., W. T. Fitts Jr., J. Gibbons and E. W. Monroe. —p. 727.
Cytologic Patterns in Benign and Malignant Gastric and Esophageal Lesions. F. G. Panico.—p. 733.
Effects of Known Compression Forces on Fracture Healing. Z. B. Freidenberg and G. French.—p. 743.
Study of Etiology of Acute Pancreatitis. M. Radakovich, H. E. Pearse and W. H. Strain.—p. 749.

Cancer of Breast: Frequency and Mortality.—The records of patients with cancer of the breast treated at the Hospitals and Clinics of the University of California from 1918 to 1947 were reviewed. The analysis included 1,056 women with primary carcinoma of the breast. Patients with other mammary neoplasms such as sarcoma were not included. Men with breast cancer and women with recurrent carcinoma of the breast were also excluded. The cases were divided according to their anatomical stage into four groups. The five year survival rate of 280 women with disease localized to the breast (stage 1) was 72.5%. In 270 women with metastases to the axillary lymph nodes (stage 2) it was 42.2%. In 250 women with advanced disease (stage 3), the five year survival was 18.4%, and none of 99 women with distant metastases (stage 4) was alive five years after admission. The five year survival rate of all 899 women was 40.4%. The data were compared with results reported from three other surgical centers in the United States and in Edinburgh. No significant differences were found. Survival of women with cancer of the breast depends on the anatomical extent of the disease at time of treatment, which is determined primarily by the biological properties of the neoplasm and possible host-resistance factors, and by the delay from apparent onset to treatment. Age at onset and operation, location of the neoplasm in the breast, and delay do not affect significantly the five year survival when the cases are grouped by the stages of the disease. If all patients had delay of less than one month from apparent onset to treatment, a five year survival of 60% could be achieved. This is 20% above the actual 40% obtained in this series, and 40% above the 20% survival to be anticipated among women with untreated breast cancer.

Antibacterial Substances in Human Semen and Prostatic Fluid.—This study was undertaken to determine the antibacterial activity of human semen and prostatic fluid against a number of common genitourinary tract pathogens and to ascertain the nature of these inhibitory factors. Semen was collected from six normal healthy medical student donors and from 13 healthy persons who brought samples in for analysis in the sterility clinic. The samples were allowed to liquefy for four hours and were used directly, or were frozen and stored in the deep freeze at -15 F (-26 C) for future experimentation. Prostatic fluid was collected from 50 persons by prostatic massage. These 50 subjects included some persons without genitourinary disease and patients who had cystitis, prostatitis, benign prostatic hypertrophy, and carcinoma of the prostate. There appear to be two antibacterial factors in human semen and prostatic fluid. It was found that one of these factors is heat stable, resisting temperatures up to 100 C for 30 minutes, and it is not extracted from test material by acid alcohol. It possesses antibacterial activity for Staphylococcus aureus, Escherichia coli, Neisseria gonorrhoeae, Neisseria meningitidis, and Bacillus cereus. The other factor is relatively heat labile, being completely inactivated at 100 C for 10 minutes. It is extracted from semen and prostatic fluid by acid alcohol solution, and its primary inhibitory action is against Micrococcus lysodeikticus. This factor is lysozyme or a lysozyme-like substance. This inhibitory activity of semen may be important in genitourinary infections such as prostatitis due to Staphylococcus aureus and gonococcal infections.

U. S. Armed Forces Med. J., Washington, D. C.

3:811-964 (June) 1952. **Partial Index**

Use of Cortisone in Dupuytren's Contracture. S. J. Ritchey.—p. 811.
Rheumatic Carditis and Hemorrhagic Pneumonitis Treated with ACTH: Report of Fatal Case. C. E. Shopfner and M. Seife.—p. 819.
Cold Injury. S. H. Horton.—p. 825.
Duodenal Ulcer in Military Personnel: Studies on Military Effectiveness of Ulcer Patient. II. Magnitude of Problem. E. L. Hamilton, B. H. Sullivan Jr. and E. D. Palmer.—p. 831.
Use of Corticotrophin (ACTH) and Cortisone in Urticaria and Dermatitis Venenata. G. H. Ekblad.—p. 839.
Influenza Type B.: Report of 12 Cases. J. A. Henderson and J. F. Tracey.—p. 847.
Cardiovascular Problems of Ambulatory Servicemen. W. H. Wehrmacher. —p. 861.
*Foreign Body Granulomas Associated with Traumatic Neuroma. A. Raftery.—p. 869.
Atypical Eczema Vaccinatum. I. L. Hoffman.—p. 885.
Primary Intestinal Tuberculosis. E. Cavin.—p. 903.
Hemangioblastoma of Central Nervous System. C. E. Buck and A. Steer. —p. 907.
Reactivity of Cardiolipin Antigens. In Yaws and in Random Group of Serums. F. Innella.—p. 917.
Medical Aspects of Tactical Atomic Warfare. H. A. Noe.—p. 939.
Evaluation of Rapid Heterophile Antibody Slide Test. F. J. Glassy. —p. 947.

Foreign Body Granulomas and Traumatic Neuroma.—Raftery says that in a study of 900 traumatic neuromas observed by one investigator in the European theater in World War II, granulomatous reaction to foreign bodies was observed in 51%. Clothing, dirt, sand, and grease were the materials most commonly encountered in wounds of the extremities. This paper reports the results of microscopic studies on 33 traumatic neuromas occurring as a result of peripheral nerve injuries in Korea. Foreign body granulomas were found in 26 of the 33 cases. The foreign bodies were of three types: cotton fibers from clothing, crystalline material resembling silica, and amorphous material. Careful débridement of wounds containing such foreign material will decrease the incidence of foreign bodies and the resultant granulomatous inflammation detrimental to nerve healing.

FOREIGN

Acta Clinica Belgica, Brussels

7:101-228 (No. 2) 1952. **Partial Index**

*Bronchopulmonary Neoplasms: Statistical Study of 100 Cases. F. Van Goidsenhoven and R. De Graeve.—p. 101.
Pure Pulmonary Stenosis. F. S. P. Van Buchem, J. Nieveen, B. Homan and J. B. Verhey.—p. 124.
Influence of Protamine Sulfate on Blood Coagulation. M. Verstraete and R. Verwilghen.—p. 139.
Regenerative and Reserve Capacity of Liver and Possible Value of this Factor in Surgery of Biliary Tract. L. Schalm.—p. 156.

Bronchopulmonary Neoplasms.—The records of 100 patients with malignant bronchopulmonary tumors who were treated at a Louvain Clinic from 1947 to 1950 are reviewed. This study confirms once more the inadequacy of treatment in most cases of bronchopulmonary carcinoma, chiefly because the diagnosis is made too late. The author lists the following factors as the chief causes of delayed diagnosis: 1. The early symptoms are not characteristic. The public is largely ignorant of the frequency of bronchopulmonary neoplasms and often several months elapse before patients consult their physician. 2. Many physicians give inadequate attention to the rather vague incipient symptoms and neglect an early roentgenologic examination. Every respiratory symptom of obscure etiology in persons of the cancer age requires immediate roentgenologic examination of the chest. 3. The complexity of the roentgenograms, often misinterpreted, has also retarded a correct diagnosis in some patients. Practitioners and specialists must continue their investigations in cases in which bronchopulmonary neoplasm is suspected until a definite diagnosis has been established; this is nearly always possible. An exploratory thoracotomy, followed by pneumonectomy if necessary, should then be carried out, unless contraindicated by evident metastasis.

British Journal of Experimental Pathology, London

33:105-216 (April) 1952

Effect on Experimental Tuberculosis and Other Infections of Micrococcin-Triton Solution. N. G. Heatley, J. L. Gowans, H. W. Florey and A. G. Sanders.—p. 105.
Radiographic Study of Tissue Permeability and Lymph Drainage in Inflammation. G. R. Barer.—p. 123.
Studies on Mechanism of Shock: Carbohydrate Metabolism in Nucleotide and Ischaemic Shock. H. B. Stoner, C. J. Threlfall and H. N. Green.—p. 131.
Acquired Resistance in Mice to Neurotoxic Action of Influenza Viruses. R. R. Wagner.—p. 157.
*Kidney Function and Structure in Chronic Fluorosis. A. M. Bond and M. M. Murray.—p. 168.
Use of Empty Bacterial Membranes in Study of Adsorption of Staphylococcus K Phage upon Its Host. J. E. Hotchin, I. M. Dawson and W. J. Elford.—p. 177.
Spontaneous Enterococcal Disease of Mice and Its Enhancement by Cortisone. A. W. Gledhill and R. J. W. Rees.—p. 183.
Antitoxic Activity and Gamma Globulin Distribution in Fractionated Diphtheria and Tetanus Antitoxin of Equine Origin. L. Levine.—p. 190.
Effect of Calcium and Electrolytes on Enzymic Action of Influenza Viruses and V. Cholerae Extract. B. M. Porterfield.—p. 196.
Comparison of Acute Toxic Effects of Iodides and Thiourea Derivatives. W. R. Trotter.—p. 202.
Deposition of Sr^{89} in Rabbit Bones Following Intravenous Injection. M. Tutt, B. Kidman, B. Rayner and J. Vaughan.—p. 207.

Kidney Function and Chronic Fluorosis.—In studies on endemic fluorosis in man due to high fluorine content of the drinking water, attention has been centered on the teeth and bone changes, but some observers also found impaired kidney function. Bond and Murray describe their own investigations on the effects of the intake of small amounts of sodium fluoride on kidney structure and function in rats. They hoped to find some means of testing for the toxic effects of fluorine in human beings and of demonstrating the existence of a fluorine hazard before severe intoxication had resulted in disability and skeletal lesions. The studies extended over a number of years and involved a large number of control and experimental rats. Rats given small amounts of NaF in the diet showed, in addition to the well-known skeletal and dental lesions, marked polydipsia and polyuria. The urine of these rats was of low specific gravity. There was slight glycosuria after 18 hours of fasting with blood sugar levels of 70 to 80 mg. per 100 ml. Administration of glucose intraperitoneally produced definite glycosuria at blood sugar levels less than 125 mg. per 100 ml. Thus there was a low kidney threshold. At autopsy the kidneys were dark, shrunken, and nodulated. Demonstration of alkaline phosphatase showed that there were fibrotic lesions in the cortex, where the enzyme was almost absent owing to absence of functional tubular tissue. Histological examination indicated that there was a vascular, glomerular, and more obviously tubular degeneration leading finally to interstitial fibrosis. The fluoride-fed rats showed diminished growth, low body weights, and diminution of fat stores. Nitrogen metabolism was greater in the fluoride-fed rats than in the controls.

British Journal of Ophthalmology, London

36:225-280 (May) 1952

Stereoscopy—and a New Stereoscope. H. Asher and F. W. Law.—p. 225.
Dacryocystorhinostomy by Intubation. W. H. Summerskill.—p. 240.
Pathological Study of Retinoblastoma Treated by Radon Seeds and Radium Disks. H. B. Stallard.—p. 245.
Improved Illumination in Indirect Ophthalmoscopy. O. E. E. Anderson.—p. 255.
Influence of Sympathetic Nervous System on Intra-Ocular Pressure and Vascular Circulation of Eye. D. P. Greaves and E. S. Perkins.—p. 258.
Anatomical Study of Schlemm's Canal and Aqueous Veins by Means of Neoprene Casts: Part II. Aqueous Veins. N. Ashton.—p. 265.

British Journal of Surgery, Bristol

39:385-480 (March) 1952

Abdominal Wounds in Jungle Warfare. J. A. Baty.—p. 388.
Mechanism, Reduction Technique, and Results in Fractures of Os Calcis. P. Essex-Lopresti.—p. 395.
*Tuberculous Disease of Breast. K. C. McKeown and K. W. Wilkinson.—p. 420.
Adamantinoma of Tibia: Report of Case. V. S. Mangalik and R. M. Lal Mehrotra.—p. 429.
Recurrent 'Nodular Goitre' in Children. R. H. Heptinstall and A. Porritt.—p. 433.
Observations on Fractures of Neck of Femur. J. Walley.—p. 441.
Acute Perforation in Regional Enteritis. J. G. Gow and A. Walsh.—p. 445.
Sudden Death Caused by Tumour Embolus in a Child of Four Years Following Operative Removal of Suprarenal Carcinoma. R. McL. Todd.—p. 447.
Dermatofibrosarcoma Protuberans. P. Borrie.—p. 452.
Cervical Neurofibroma in Differential Diagnosis of Carotid Body Tumour. T. H. Cullen and R. S. Monro.—p. 454.
Alkaline Phosphatase in Breast Carcinomas. J. M. Drennan.—p. 458.
Case of Haemangiomatosis of Small Intestine. P. P. Rickham.—p. 462.
Self-Inflicted Stripping of Rectal and Colonic Mucous Membrane. B. N. Catchpole.—p. 464.

Tuberculous Disease of Breast.—At the Mayo Clinic 0.51% of all breast lesions seen during the decade ending in 1915 were tuberculous, and at St. Bartholomew's Hospital, London, 1.5% of 1,500 breast lesions were tuberculous. Possible routes of infection are hematogenous spread, direct inoculation, ductal infection, spread from contiguous structures, and lymphatic spread. The breast lesions may be of the following types: acute miliary, nodular, disseminated, sclerosing, and obliterating. Atypical types occur, and the lesion may be associated with carcinoma. The infecting organism is usually of the bovine type. Two of the five cases discussed illustrate the "primary" type of tuberculous mastitis, occurring in young married women under the age of 30. In both cases the disease occurred in association with pregnancy, and in both a clinical diagnosis of breast abscess was made. The general health in these two patients was good, and there was no history of previous tuberculosis. Excision of the breast led to complete cure. The origin and route of infection was not clear, but the fact that the lesions occurred so near the areola suggests the possibility of ductal infection. The other three patients had the secondary type of tuberculous mastitis. In this type surgical treatment is limited to such measures as curettage and excision of sinuses. Localized surgical measures may prove adequate if the response to streptomycin and *p*-aminosalicylic acid is favorable. Without treatment the disease progresses; spontaneous regression has not been reported. Differentiation from cancer is facilitated by the fact that tuberculous

mastitis usually occurs at an earlier age and progresses with greater rapidity than cancer. Pain is more marked in tuberculous mastitis, and axillary glandular enlargement occurs more frequently and earlier in the course of the disease. Actinomycosis may resemble disseminated tuberculous mastitis, but the occurrence of sulfur granules and identification of the fungus will differentiate actinomycosis.

British Medical Journal, London

1:1145-1206 (May 31) 1952

Cortisone in Rheumatic Carditis: Some Preliminary Observations. E. N. Chamberlain, J. D. Hay and D. M. Freeman.—p. 1145.
Some Concepts of Rheumatic Disease. J. H. Kellgren.—p. 1152.
Prevention of Streptomycin Resistance by Combined Chemotherapy. A Medical Research Council Investigation.—p. 1157.
*Chemotherapy of Pulmonary Tuberculosis in Young Adults: Analysis of Combined Results of Three Medical Research Council Trials. M. Daniels and A. B. Hill.—p. 1162.
Kernicterus Without Prematurity or Blood-Group Incompatibility. N. R. Butler and W. G. Spector.—p. 1168.
*Study on A Factor as Cause of Haemolytic Disease in Premature Babies. S. Phansomboon and O. J. Pollak.—p. 1170.
Peculiar Syndrome of "Bladder Paralysis" in Natives of South Central Africa. M. Gelfand and E. E. Barnett.—p. 1172.
Relief of Acute Left Ventricular Failure by "Priscol." D. Wheatley. —p. 1174.

Chemotherapy of Pulmonary Tuberculosis.—From 1947 to 1951 three trials of chemotherapy of pulmonary tuberculosis in young adults were made under the direction of the Medical Research Council. A detailed analysis of the combined results of these trials has been presented as follows: There were 388 patients between the ages of 15 and 30 who had similar forms of acute progressive bilateral pulmonary tuberculosis that was believed to be of recent origin, bacteriologically proved, and unsuitable for collapse therapy. Fifty-two were treated by rest in bed only, 109 by streptomycin alone in doses of 1 or 2 gm. daily, 59 by *p*-aminosalicylic acid alone, 73 by streptomycin in doses of 1 gm. daily combined with 5 or 10 gm. of *p*-aminosalicylic acid daily, and 95 by streptomycin in doses of 1 gm. daily combined with 20 gm. of *p*-aminosalicylic acid daily. The results six months after the start of treatment were much better in all groups receiving chemotherapy than in the group treated by rest in bed alone. They were much better in the groups receiving streptomycin than in those given *p*-aminosalicylic acid only, and better in the group receiving combined therapy than in those receiving streptomycin alone. There was no apparent difference between the groups given different daily doses of *p*-aminosalicylic acid in addition to 1 gm. of streptomycin daily. There was no difference between the results in men and those in women. The percentage of patients with bacteria strains that developed streptomycin resistance was much higher among those treated with streptomycin alone than in those receiving combined therapy; among the latter it was higher in patients who were given a daily dose of 5 or 10 gm. of *p*-aminosalicylic acid than in those receiving 20 gm. of this drug daily. Assessment of the clinical significance of bacterial drug resistance has been difficult. Clinical results were better in patients in whom resistant strains did not develop. Analysis showed that, regardless of the initial clinical condition, the prognosis was generally adversely affected by the emergence of strongly resistant organisms. Moderate drug resistance seemed to be much less significant.

Factor A and Hemolytic Disease.—Two serologically and microscopically proved cases of isoimmunization to the A factor are reported that resulted in the birth and neonatal death of infants suffering from erythroblastosis. In the first case, sensitization to the A_1 factor occurred during the first pregnancy of a 19-year-old woman, and in the second case sensitization to the intermediate A_1-A_2 type occurred in the third pregnancy of a 26-year-old woman. In case 2 differentiation between the A_1, intermediate A_1-A_2, and A_2 factors was required, and was shown by the difference in quantitative titration of immune A antibodies with red cells of intermediate A_1-A_2 type. Without serologic investigation, neonatal death from fetal erythroblastosis resulting from isoimmunization to the A-B factors may often be recorded as due to prematurity and atelectasis.

Encéphale, Paris

41:217-312 (No. 3) 1952

*Electroencephalography in Brain Tumors with Psychological Symptoms. J. Delay, G. Verdeaux and R. Marty.—p. 217.
Experimental Research on Clinical Use of Szondi's Test. A. L. Kobler. —p. 234.
Psychological and Therapeutic Aspects of Intermittent Stimulation with Light; "Stimulated Subnarcosis." J. Faure.—p. 243.
"Subacute Necrotic Myelitis." P. C. van Reeth.—p. 289.

Electroencephalography in Brain Tumors.—Psychological disturbances during formation of intracranial neoplasms occasionally may dominate the clinical picture, and the patients may therefore be examined only from this point of view. Thus in practice they are subjected to examination by a psychiatrist, and it will be his task to detect the cause of the syndrome and to consider a neurosurgical intervention. The authors report four cases of this type in men between the ages of 19 and 57 in whom the electroencephalogram revealed abnormal brain waves, particularly slow waves of delta rhythm, suggesting the presence of an intracranial neoplasm, which was confirmed by surgical intervention. There is a much larger number of cases collected from the literature in which electroencephalography was performed to confirm the suspected presence of an intracranial tumor. Thus electroencephalography steadily gains in importance among the examinations required for diagnosis of a brain tumor. In the presence of mental manifestations of a suspected neoplasm, electroencephalography as well as roentgen examination of the cranium and examination of the eyeground should be included in the study of the patient.

Journal of Clinical Pathology, London

5:129-224 (May) 1952

Vitamin B_{12} Concentrations of Serum and Urine of Normals and of Patients with Megaloblastic Anaemias and Other Diseases. D. L. Mollin and G. I. M. Ross.—p. 129.
Studies on Pathogenesis of Thalassaemia. G. Astaldi and P. Tolentino. —p. 140.
Bone Marrow in Anaemia of Pregnancy. J. M. Scott and A. D. T. Govan.—p. 145.
Diagnosis of Carriers of Cooley's Anaemia. F. S. Mooney.—p. 154.
Starch-Fermenting, Gelatin-Liquifying Corynebacteria and Their Differentiation from C. Diphtheriae Gravis. G. T. Cook and W. H. H. Jebb. —p. 161
Antibiotic Sensitivity of Pathogenic Staphylococci. W. D. Linsell.—p. 165.
Incidence of Antibiotic Resistance in Gram-Negative Bacilli in General Hospital. E. F. Thomson.—p. 169.
Coronary Arteriosclerosis and Calcification in Infancy. R. A. Sladden. —p. 175.
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Serum Copper and Its Relationship to Serum Iron in Patients with Neoplastic Disease. R. Pirrie.—p. 190.
Blood Serum Protein-Bound Carbohydrate After Injury. J. W. Keyser. —p. 194.
Intrathecal Streptomycin and Cerebrospinal Glucose Estimation. M. J. H. Smith.—p. 199.
Cholesterol Tolerance Test in Normal Individuals. N. I. Fahmy and P. Ghalioungui.—p. 203.

Lancet, London

1:1077-1122 (May 31) 1952

First Part of Duodenum. H. Ogilvie.—p. 1077.
Analysis of Reports on Infusion of Dextran Solution. W. D'A Maycock. —p. 1081.
Salicylates and Neuro-Endocrine Stimulation. H. Van Cauwenberge and H. Betz.—p. 1083.
*Late Prognosis in Acute Tubular Necrosis; Interim Follow-Up Report on 14 Patients. K. G. Lowe.—p. 1086.
Weil's Disease: Cautionary Tale. P. J. O'Connell and J. C. Broom. —p. 1088.
Paracolon Bacillus Septicaemia. R. J. Kernohan.—p. 1090.
Nephrotic Syndrome Complicating Tridione (Troxidone) Therapy. J. D. N. Nabarro and M. L. Rosenheim.—p. 1091.
Effect of Dimercaprol on Hypertension. J. H. Baylis and R. Kauntze. —p. 1092.
Fate of Face in Poliomyelitis. E. W. Moore.—p. 1092.

Late Prognosis in Acute Tubular Necrosis.—Of 40 patients treated since 1947 for anuria or severe oliguria due to tubular necrosis, 26 have recovered. Only 14 of these 26 were followed as outpatients, and some have been followed for three years. All had had severe episodes of renal failure, with periods of anuria or oliguria lasting from one to three weeks and peak blood urea levels of 300 to 500 mg. per 100 ml. In general all 14 patients made a good clinical recovery from their acute illness and sub-

sequently were in good health. Without exception they had returned to their previous employment or to full household duties. On physical examination some of the random blood pressures were above the normal range. The significance of this was difficult to assess, because the circumstances of outpatient attendance were not such as to provide basal conditions. Results of renal function tests showed that there usually was good recovery of renal function within the first six months, but renal function tended to remain below the lower limit of normal. One woman who was followed had an uneventful pregnancy three years after her episode of renal failure, and two who were not followed as outpatients had subsequent normal pregnancies.

Medical Journal of Australia, Sydney

1:533-556 (April 19) 1952

Avicenna. W. S. Dawson.—p. 533.
Barotrauma. N. E. H. Box.—p. 538.
Succinylcholine Chloride: An Ultra-Short-Acting Relaxant. A. P. Balthasar and C. A. Sara.—p. 540.
Additional Note on Simple Method for Estimation of 17-Ketosteroids in Urine. V. I. Krieger.—p. 542.

1:557-592 (April 26) 1952

Obstetrics Through the Ages. L. Townsend.—p. 557.
Carcinoma of Bronchus: Problem of Early Diagnosis. A. H. Penington.—p. 565.
Leprosy Among Full-Blooded Aborigines of the Northern Territory. A. H. Humphry.—p. 570.
Chronic Aregenerative Anaemia of the Newborn. D. E. Anderson.—p. 573.

Minerva Dermatologica, Turin

27:41-64 (March) 1952. **Partial Index**

Skin Manifestations of Beryllium Intoxication. A. Midana.—p. 41.
Plasma Proteins in Pemphigus: Iontophoretic Study. L. Ricciardi.—p. 44.
*Trial Treatment of Lupus Vulgaris and Common Acne with Provitamins D. B. Cerri.—p. 53.

Provitamins D in Therapy of Lupus Vulgaris and Common Acne.—Results are reported of provitamin D therapy in seven patients with lupus vulgaris and six with common acne. During therapy the patients were given milk or, when this was not tolerated, calcium by mouth. Provitamin D_2 was given for 8 to 10 weeks, in a total dose of from 738 mg. to 3,334 mg. to three patients with lupus vulgaris. There was no improvement. Provitamin D_3 was given for 4 to 11 weeks, in a total dose of from 1,680 mg. to 3,960 mg. to the other patients with lupus vulgaris. There was a mild improvement in one patient, who also gained some weight. Three patients with common acne treated with a weekly dose of 45 mg. of provitamin D_2 for 5 weeks and one treated with a weekly dose of 45 mg. of provitamin D_3 for 12 weeks did not improve. A pronounced and lasting improvement occurred in one patient with common acne to whom provitamin D_3 was given first in a weekly dose of 45 mg. for 1 week, then 30 mg. for 3 weeks, and finally 15 mg. for 11 weeks. Another patient with common acne in whom roentgenograms revealed right exudative pleurisy received 360 mg. of provitamin D_3 weekly for four weeks. The general condition and the dermatitis improved, the pleurisy was cured, and the patient gained weight. Thus, mild results were obtained with provitamin D_3 only. Although provitamins never caused side-effects even when massive doses were given, their use in therapy of these skin diseases is not recommended because the results are inferior to those that can be obtained with vitamin D_2 (calciferol).

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

96:1121-1184 (May 10) 1952. **Partial Index**

Hypertension in Unilateral Renal Lesions (Van Houtum-Goldblatt). A. W. Griep.—p. 1132.
*Diathermic Coagulation in Treatment of Premenopausal Hemorrhages and in Uterine Carcinoma. B. S. ten Berge.—p. 1136.
*Atrophy of Small Hand Muscles as Result of Cardiac Infarct. P. J. Zuidema.—p. 1141.
Results of Pulmonary Resection in Bronchiectasis. L. D. Eerland and R. R. Swinnen.—p. 1145.
Treatment of Hyperchromic Anemia. S. I. de Vries.—p. 1150.

Diathermic Coagulation for Premenopausal Hemorrhages and for Uterine Carcinoma.—B. S. ten Berge says that at his clinic efforts have been made since 1930 to develop a method of coagulating the uterine mucosa of women with premenopausal menorrhagia and metrorrhagia by means of diathermic current. Extensive preliminary studies were made on animals, and devices were constructed that made it possible to coagulate the uterine mucosa with a diathermy current at about 60 C, this temperature being controlled by means of a pyrometer constructed by French technicians. Diathermic coagulation arrests uterine hemorrhage but does not impair the function of the ovaries. This method can be employed in the treatment of acute profuse hemorrhages, which are quickly arrested. Coagulation of the uterine mucosa at the higher temperature of 80 C influences deeper mucosal layers and is helpful as a preoperative measure in cases of uterine cancer, since it will prevent dissemination of cancer cells during operation. This method of diathermic coagulation has been employed by ten Berge during the last 10 years. It proved effective, and it is harmless and easy to carry out.

Atrophy of Small Hand Muscles as Result of Cardiac Infarct.—Zuidema presents the case of a man, aged 37, who was hospitalized because of cardiac infarct. Several months after the cardiac infarction, atrophy of the small muscles of the right hand became evident and did not improve. Other symptoms of the shoulder-hand syndrome that sometimes results after coronary thrombosis could not be demonstrated. It appears that prolonged irritation arising from the ischemic heart muscle produced a degeneration of the motor cells of the anterior horn at the level of the seventh and eighth cervical nerves.

New Zealand Medical Journal, Wellington

51:65-148 (April) 1952. **Partial Index**

Subacute and Chronic Hepatitis. J. A. K. Cuningham.—p. 69.
Sudden and Unexpected Deaths. F. J. Cairns.—p. 74.
Cytological Diagnosis of Uterine Carcinoma. J. F. Burton.—p. 82.
*Forced Thinking as Part of Epileptic Attack. I. M. Allen.—p. 86.
Disturbed Diaphragmatic Movement. D. A. Ballantyne.—p. 95
Swineherd's Disease in New Zealand: Infection with Leptospira Pomona in Man, Calves and Pigs. L. Kirschner, T. F. Miller and C. H. Garlick.—p. 98.
Rupture of Spleen in Infectious Mononucleosis: Report of Case. C. H. Belton.—p. 111.

Forced Thinking in Epileptic Attacks.—Compulsive thought or forced thinking was a prominent feature of attacks in 10 of a series of 500 patients with epilepsy. The forced thinking was compulsive and beyond the control of the patient. The content of the forced thinking was recalled after the attack in only two cases. To ascertain the site of the initial discharge in cases in which forced thinking was the initial or an early symptom of the epileptic attack, the author analyzes the symptoms that preceded, accompanied, or followed the forced thinking and the symptoms that did not appear at all before, with, or after it. He found that the initial discharge is not in those areas of the temporal lobe from which the various forms of dreamy state are produced, but must be in that part of the frontal lobe near the middle line, in front of the precentral gyrus and an appreciable distance behind the frontal pole. It must be unilateral rather than bilateral, for attacks with forced thinking only, with forced thinking followed by a lapse in consciousness of varying duration, or with sudden loss of consciousness and no forced thinking were equally common in the persons affected. Bilateral discharge or one appearing in both cerebral hemispheres, from or through a firing point in the diencephalon, would be associated invariably with loss of consciousness. It was always left-sided in the cases in which there was an indication clinically of the side on which the discharge occurred. Evidence so far available suggests that forced thinking occurs not as a direct effect of the initial discharge but as an indirect effect due to release from higher control of lower but still complex levels of integration responsible for the content of the thought and its emotional accompaniments. The level released is a higher one than that released when coordinated and integrated movements are the chief expression of the automatism.

Practitioner, London

168:453-550 (May) 1952. **Partial Index**

Anomalies of Pigmentation. G. B. Dowling and F. A. Whitlock.—p. 453.
Keloids and Their Treatment. B. Solomons.—p. 465.
Neurodermatoses. H. R. Vickers.—p. 473.
Dermatitis Artefacta. E. C. Ritter.—p. 480.
Diseases of Scalp and Hair. O. L. S. Scott.—p. 487.
Malignant Diseases of Skin. H. Gordon.—p. 498.

Presse Médicale, Paris

60:741-760 (May 17) 1952. Partial Index

*Permeability Tests of Surgical Anastomoses of Portal and Caval Systems. L. Leger, J. Patel, P. Castaigne and G. Ferbos.—p. 741.
Problem of Cervical Cancer in Stage Zero. G. Gricouroff.—p. 743.
Egg-Yolk Broth in Infant Feeding. M. Pestel.—p. 746.

Permeability Tests of Surgical Anastomoses of Portal and Caval Systems.—An ideal test for determining the permeability of portacaval shunts has yet to be found; those now in use have various disadvantages. Radiography of the anastomosis using a contrast medium, direct or indirect measurement of the portal pressure, and comparison of the blood chemistry of the portal and caval systems all require catheterization of the inferior vena cava, which is not always convenient or even possible. Efforts to avoid catheterization by measuring humoral changes resulting from exclusion of the liver are open to objection, either on the ground that the changes are due to some other cause or that the measurements are subject to error. Measurement of the portal circulation time, i. e., the period elapsing between the intraduodenal injection of 1 cc. of ether mixed with 5 cc. of isotonic sodium chloride solution cooled to 4 C and its gustatory perception is perhaps the most convenient and reliable test available at present. Attempts to clarify the physiological changes brought about by a portacaval shunt and to establish its permeability will undoubtedly help to define the indications for the operation and may lead to a fuller comprehension of the underlying pathogenesis.

Schweizerische medizinische Wochenschrift, Basel

82:561-584 (May 24) 1952. Partial Index

*Experimental Production of L. E. Cells. T. Inderbitzin.—p. 561.
*Psychic Effects of Treatment with Sex Hormones. E. H. Hauser.—p. 566.
"Senseless" Questions on the Part of Patients. P. Parin.—p. 568.
Preoperative Prothrombin Values in Hyperthyroidism. U. G. Müller-Handschuh.—p. 572.
Skin Necroses in Diabetic Patient Produced by Insulin. H. Bartelheimer.—p. 573.

Experimental Production of L. E. Cells in Normal Blood.—In an earlier report Inderbitzin had reported on the production of phagocytic manifestations of leukocytes when blood coagulation was inhibited by the heparin-like preparation sodium polyanetholsulfonate ("liquoid"). The phagocytizing, predominantly polynuclear, leukocytes showed a surprising morphological similarity to the L. E. cells. This report describes additional experimental results on the artificial production of these phagocytic manifestations in leukocytes in human as well as in animal (rabbit) blood. In addition to heparin and polyanetholsulfonate, a third anticoagulating substance, the sodium salt of a polyvinylalcohol-polysulfuric acid ester, was studied with regard to its action on leukocytes. It was found that the phagocytic phenomenon in the form of L. E. cell formation can be produced by synthetic substances that induce blood coagulation in human and in animal blood. The phenomenon can be produced in vitro by adding the coagulant substance to blood as well as in vivo by intravenous injection of the anticoagulant. In the latter case temporary leukocytosis results. During the phase of the increase in leukocytes, destruction of the polynuclear cells predominate, and during the phase of decrease the phagocytic processes appear. In the case of one of the synthetic anticoagulants (polyanethalsulfonate), the phagocytosis involves particularly thrombocytic material and phagocytosis of the nuclear mass plays only a subordinate role. The latter predominates, however, if the other synthetic anticoagulant is used. The hypothesis is advanced that the formation of L. E. cells in acute lupus erythematosis is connected with the appearance of pathologic heparinoids, the development of which is possibly connected with impairment of the collagen.

Psychic Effects of Sex Hormones.—When patients with carcinoma are treated with large doses of the hormones of the opposite sex, an effect is noticeable on the general mood, particularly the sexual drive. Other drives may be influenced to a lesser extent; for instance, there may be an increase in appetite. In women the sexual drive is generally increased, and sometimes leads to masturbation, whereas in men it is reduced. In a few women, however, there is no effect on the sex drive or it may even be lessened. One woman had the sensation that she was becoming hermaphroditic, probably because of hirsutism. All women who complained about increased sex drive believed it was pathological and foreign to their character. The reduction of sex drive in men was regarded as annoying by only two of the men. The psychic effect of sex hormones is inconstant and cannot be estimated in advance. There is only a slight correlation between psychic and physical hormone action. The intensity and rapidity of development of the hormonal effects seem to be determined largely by the constitution and disposition of the individual. Treatment with sex hormones in large doses produces temporary euphoria in nearly all depressed persons. In a few cases the depression is permanently relieved, but the possibility of spontaneous improvement should not be overlooked. Administration of sex hormones nearly always affects the depressive mood. In a few cases the depression is temporarily intensified by hormone therapy. In one woman with greatly increased androgen formation in the presence of hypernephroma, mental and physical changes were observed that were similar to those following the injection of sex hormones.

Tubercle, London

33:131-158 (May) 1952

Tuberculous Peritonitis: Follow-Up Study of 169 Cases. T. Kahrs.—p. 132.
Benemid and Sodium PAS. F. A. H. Simmonds and E. V. Hess.—p. 138.
Two Cases of Spontaneous Pneumothorax Complicating Artificial Pneumoperitoneum. J. S. Miller.—p. 143.
Oxalic Acid and Acid-Iron-Peroxide in Routine Culture of Tubercle Bacilli from Sputum. C. H. Collins.—p. 149.

Zeitschrift für Kinderheilkunde, Heidelberg

70:535-650 (No. 6) 1952. Partial Index

Influence of Sympathetic Irritation on Dynamics of Heart of Child. T. Hockerts.—p. 535.
Protrusion of Epiphysis at Medial Malleolus in Ricketts (Marfan's Symptom). P. K. Lüttgens.—p. 541.
Fluorescence Microscopy of Blood Cells. H. M. Kosenow.—p. 552.
*Hypertension in Children with Unilateral Renal Disease. K. Seelemann and G. Linnekogel.—p. 568.
Changes in Serum Proteins in Nephroses and Their Significance for Therapy and Pathogenesis. K. Kropp and H. Althoff.—p. 588.
Psychological Changes in Poliomyelitis. W. Bappert.—p. 613.

Hypertension in Children with Unilateral Renal Disease.—The first of the three children whose cases are reported here was a girl, aged 9, who had congenital hypoplasia of the left kidney. Relapsing cystitis produced ascending infections, and chronic pyelonephritis resulted, probably during the fifth or sixth year of life. An increase in blood pressure presumably occurred at this time, which in turn produced changes in the right kidney and resulted in malignant sclerosis. At this time, pseudouremia developed, which led to the discovery of retinitis albuminurica in the presence of a blood pressure of 200/100. Removal of the congenitally defective left kidney could no longer produce much improvement, because the functional capacity of the right kidney had become greatly impaired as the result of irreversible vascular changes. However, death a few hours after operation was not necessarily due to this factor, but suggested the picture of shock following removal of a hyperplastic adrenal, the left adrenal having been removed together with the left kidney. The authors feel that in this case the opportune time for the only effective treatment, namely removal of the congenitally defective kidney had been missed, partly because regular determinations of blood pressure had been neglected. The second case reported here, a boy, aged 8, likewise had been born with hypoplasia of the left kidney and subsequently developed pyelonephritis, leading to early involvement of the right kidney, which in this case took the form of interstitial nephritis with abscess formation. The level of rest nitrogen was constantly increased, but the blood pressure remained normal. Two weeks before death, thrombophlebitis of the left kidney developed, which terminated with thrombophlebitic sepsis. In the third patient, an 11-year-old girl, contracted kidney and fixed hypertension had developed as the result of a pyelonephritis. After left-sided nephrectomy, the blood pressure decreased to almost normal levels. The authors stress that even hypertension of renal origin is a complex humoroneural process. The pressor substances produced by the kidney activate neural and perhaps hormonal factors, which in turn may maintain the hypertension even after the exclusion of the diseased kidney.

BOOK REVIEWS

Poisoning: A Guide to Clinical Diagnosis and Treatment. By W. F. von Oettingen, M.D., Ph.D. Cloth. $10. Pp. 524. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1952.

The increase in the number of poisonous substances in use for agricultural, industrial, household, and therapeutic purposes has been so great in recent years as to defeat the efforts of all but those with sufficient time and a compelling interest in toxicology to keep abreast with information on available compounds. The author has organized, in a convenient fashion, the pertinent facts for the diagnosis and treatment of poisoning by most of the poisonous agents that physicians are likely to encounter in general practice.

The book is divided into four parts. The first part is devoted to short chapters on the classification of poisons, medicolegal responsibilities, and a summary of emergency measures and equipment. Part two takes up in detail the clinical diagnosis of poisoning, the pathological changes of organs and their functions that may be observed during examination, the biochemical changes in the blood and urine, and laboratory tests for the detection of toxic substances or their metabolites in blood and urine. A departure from the usual content of toxicology texts is the inclusion of lists of chemicals under each sign or symptom that has been reported to cause such effects. Part three contains discussions on the management of poisoning. Chapters are directed to the rationale of treatment and techniques for aiding the removal or elimination of the toxic agent, detoxification, symptomatic treatment, and general measures for the treatment of aftereffects. Part four, on symptoms and treatment of 461 types of poisoning, constitutes the largest section of the book. Short descriptions of individual poisons are arranged alphabetically. The descriptions give a synopsis of the clinical picture and instructions for treatment for each type of poisoning. They emphasize the general symptomatology as contrasted to the discussions on individual signs and symptoms discussed in part two.

As a reference guide to help in detecting poisoning and instituting effective treatment, the book can be highly recommended. A list of types of commercial preparations, occupations, or general situations in which many of these substances are frequently encountered would add materially to the value of this book as a reference guide.

A Textbook of Histology. By Alexander A. Maximow and William Bloom, Professor of Anatomy, University of Chicago, Chicago. Sixth edition. Cloth. $10. Pp. 616, with 986 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, 1952.

The sixth edition of this deservedly popular textbook on histology has kept pace with the accumulative tempo of modern knowledge. It has been largely rewritten, exhibiting pronounced alterations in content and, in places, changes in point of view. Since there are many specialized facets in the field of histology, it is interesting to note the inclusion of a new introductory chapter that correlates the submicroscopic, biochemical, and enzymatic constitution of cells with their structure and function. Among others, the chapters on blood, connective tissue, bone, cartilage, endocrine glands, epithelium, glands, and the lymphatic system and spleen have been revised and shortened; however, most of the chapters have been shortened without deletion of essential material, especially those dealing with the eye, ear, male and female generative systems, nervous tissue, skin, muscle, and the digestive tract. New colored plates, photomicrographs in color, and electron micrographs are included. This book is a most useful tool for study and reference and is highly recommended for frequent use by medical students.

The reviews here published have been prepared by competent authorities and do not represent the opinions of any official bodies unless specifically stated.

Statistics for Medical and Other Biological Students. By L. Bernstein, B.Sc., M.R.C.S., L.R.C.P., and M. Weatherall, M.A., D.M., B.Sc. Cloth. $4. Pp. 180, with 17 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1952.

This book is designed for use in connection with a "short course of lectures and practical classes" given by the authors to medical students in their first year of preclinical studies. The statement that the authors sought in vain for the ideal textbook and decided to write a book themselves is by now a familiar refrain; it explains the appearance of many similar efforts in English and in other languages. This inevitably results from the difficulty of the subject, which defies simplification, from the varying attitudes of the classes, and from the different qualifications of the teacher. First year students are likely to be patient with the whimsical logic (page 1) whereby the present authors deduce how many legs a given dog should have, but fourth year students are likely to resent anything less practical than the interpretation of mortality tables. Students who have not taken courses in advanced algebra, genetics, or experimental psychology may still profit from the experiment in penny tossing (page 11 ff.) suggested by the authors, but others will be expecting details about correlation coefficients, self-correlation, test-retest correlations, and regression toward the mean. Collecting the necessary data and writing out the directions for a really good collection of numerical exercises or "sums" is extremely time consuming, and many teachers prefer a book that supplies this need. Since this book devotes so much space to apparently trivial things, such as swans and pennies, is so brief and abstract in its treatment of subjects like correlation, lacks numerical exercises, and omits applications like vital statistics and insurance problems, its usefulness in other schools will be limited. It is undoubtedly well adapted to the local situation, and in the hands of good teachers its accuracy, conciseness, and neat format will appeal to students.

Textbook of Clinical Parasitology. By David L. Belding, M.D. Second edition. Cloth. $12. Pp. 1139, with 283 illustrations. Appleton-Century-Crofts, Inc., 35 W. 32nd St., New York 1, 1952.

In a recent article (*Science* **115**:407 [April 18] 1952) Marston Bates remarked that "we rarely try to evaluate the (scientific) book in terms of how well it has succeeded in obtaining its objectives; we are ready to damn, but we are cautious with our praise." An attempt will be made to keep this criterion in mind in reviewing the second, greatly enlarged edition of Dr. Belding's well-known book on parasitology. The volume is comprehensive in its coverage of the animal parasites, including an introduction on general parasitology, and sections on Protozoa, Nemathelminthes, or roundworms, Cestoda, including the tapeworms, Trematoda, including the flukes, the Arthropoda, and technical methods for the diagnosis and treatment of parasitic infections. The sections are conveniently divided into major subdivisions, each of which constitutes a chapter. With few exceptions, classification of the organisms is that which is generally accepted by parasitologists.

In the text, tables, and illustrations, the material is presented with a relatively satisfactory balance between the parasites of major and those of incidental clinical importance. Also, the subheadings for each species are separated, so that the reader who is interested primarily in a particular aspect, e. g., biologic, clinical, or preventive, can find this topic without too much difficulty. The style is lucid and as nontechnical as the complexities of the material permit, although there is unnecessary duplication of information in the introduction, the chapters dealing with particular parasites, and those on diagnosis and treatment. A new chapter on insecticides and repellents, appended to the technical section, adds valuable information. This might have been appropriately placed as the concluding chapter of the section on Arthropoda. There are many bibliographic references at the end of each chapter and good author and subject indexes.

In the preface the author states that his "Clinical Parasitology is designed for medical students, physicians, medical personnel in the armed services, public health officials, laboratory

workers, and biologists." If acquaintance with the animal parasites as such is the objective, then the goal has been attained. If, however, the aim is also clinical, much remains to be achieved, since the balance weighs strongly in favor of the parasite as distinguished from its pathogenic effects on the human host and the signs and symptoms evoked. Diagnosis, of necessity based primarily on demonstration of the parasite or on immunologic tests, is fairly well discussed, although several of the more important recent diagnostic procedures are not included. In most instances there is a fairly satisfactory consideration of standard chemotherapeutic measures, but few of the newer antiparasitic drugs are mentioned. The reader is therefore deprived of valuable information on treatment with bismuth glycolylarsanilate, aureomycin, terramycin, and chloroquine in amebiasis, the extensive work with hetrazan® (1-diethylcarbamyl-4-methylpiperazine hydrochloride) in the filariases, quinacrine hydrochloride in teniasis, primaquine and amodiaquine (camoquin®) in malaria, and dieldrin as an insecticide. Reference to the epochal work of Shortt and associates on the pre-erythrocytic stages of Plasmodium vivax and P. falciparum is lacking.

One item of misleading information is embodied in the outline of intestinal amebiasis (page 97). Only two alternatives are presented, amebic dysentery and "cyst passers." The medical profession today recognizes a variety of syndromes between acute amebic colitis, which is not necessarily manifested as a dysenteric state, and asymptomatic infection.

The second edition is well printed and attractively bound. Its good points have already been mentioned. Its faults are primarily twofold. Although it bears the publication date of 1952, all the information antedates 1950. In the second place, 50% more subject matter has been added without enlarging the scope or usefulness of the book. It may be doubted that Dr. Belding has succeeded in obtaining his objective, namely, providing a text on clinical parasitology. This new edition will find a place in parasitological literature, but, in many respects, it is not as satisfactory as the 1942 edition.

Physical Medicine in General Practice, with Twenty-Two Contributors. Edited by William Bierman, M.D., and Sidney Licht, M.D. Third edition. Cloth. $12.50. Pp. 798, with 234 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1952.

The current edition of this text is a product of 2 authors and 22 contributors. It is divided into two sections; the first section deals with procedures and the physical agents and the second section with the clinical applications of physical medicine. The latter section includes material on such subjects as diseases of the locomotor system, arthritis and rheumatic diseases, the amputee, neurological diseases, anterior poliomyelitis, cardiovascular diseases, diseases of the digestive system, genitourinary diseases, gynecologic diseases, ear, nose, and throat diseases, respiratory diseases, and dermatology.

Although the book was primarily intended for the general practitioner, it includes information on techniques that he probably would not use; however, for the most part, the text contains descriptions of the employment of the standard apparatus and methods used in physical medicine and rehabilitation.

The book is complete but in some instances does not present critical evaluations of the techniques described. This will be a handicap to the general practitioner who uses this book as a reference text, as he will have difficulty deciding on the therapeutic efficacy of some of the procedures. Thus, the text may give the reader unfamiliar with this specialty the wrong impression of the modern concepts of the practice of physical medicine and rehabilitation; for example, the "Schnee" four cell baths, hydrogalvanic baths, and ultraviolet blood irradiation are considered in the text.

As the preface to this edition indicates, "The contents of the previous editions were carefully screened to eliminate sections out dated by progress in and outside physical medicine and to remove data of secondary importance in order to make room for new information and keep the volume within moderate size." In view of this it is difficult to understand the inclusion of information about an ancient, ponderous, and outmoded static machine along with indications for its use. The text is written in a readable style and is illustrated with simple line drawings. The format is attractive.

Handbuch der inneren Medizin. Band I: Infektionskrankheiten. Teile 1 und 2. Begründet von L. Mohr und R. Staehelin. Herausgegeben von G. v. Bergmann, W. Frey, H. Schwiegk. Fourth edition. Cloth. 204 marks; 299 marks. Pp. 1536, with 417 illustrations; 1225, with 293 illustrations. Springer-Verlag, Reichpietschufer 20, Berlin W. 35 (West-Berlin); Neuenheimer Landstrasse 24, Heidelberg; Göttingen, 1952.

In American terminology both this book's size and its contents place it in the reference-book class. Part 1 of this volume contains only part of the material on the infectious diseases. The editors are well-known clinicians, and the contributors have been carefully chosen for their special knowledge of the fields they discuss. The volume opens with a consideration of the general principles governing epidemiology by Drs. Hans Schlossberger and I. Eckard of Frankfurt on the Main. This chapter, like the others, is followed by a bibliography. Chapter 1 is followed by discussion of the common exanthems of childhood and some rarer infections. The chapters on tropical virus diseases were written by Prof. E. G. Nauck of Hamburg. These include yellow fever, dengue, sand fly fever, and rift fever. A general discussion of the rickettsial diseases by Professors Aschenbrenner of Hamburg and Eyer of Bonn follows. There is a discussion of the clinical aspects of the typhus fever group, trench fever, and Q fever, and there are chapters on the rarer infections by Professors Mohr and Enigk of Hamburg. The mycoses are discussed by Dr. Mohr, who considers the mucormycoses, coccidiomycosis, rhinosporidiosis, the blastomycoses, aspergillosis, toxomycosis of the lung, sporotrichosis, moniliasis, histoplasmosis, geotrichosis, nocardiosis, and the actinomycosis group.

Chapters on the septic diseases, emphasizing their pathology and pathogenesis and their foci of origin, are contributed by Dr. Bingold of Munich. Professor Hottinger of Basel covers the various forms of acute throat inflammation, his clinical description being preceded by a consideration of definitions, the significance of disposition, the anatomy, physiology, bacteriology, and biochemistry of the tonsils, focal infection, and the frequency of the different forms of angina. In this section chronic tonsillitis, tumors of the tonsils, and a discussion of diagnosis is included. Infectious mononucleosis is then considered by Professor Glanzmann of Bern, diphtheria by Dr. Hottinger, meningococcus infections by Dr. O. Gsell of St. Gallen, and typhoid and paratyphoid fever by Dr. Bingold. The book is printed on a good quality of paper; the typography is excellent; and the illustrations, many in the form of charts and some in color, are enlightening. The text is systematically arranged and clearly written; there is a good bibliography after the discussion of each disease. The work is a worthy successor to the original Mohr and Staehelin's system and is a valuable reference work.

Part 2, like part 1, is concerned with infectious diseases, and the final 217 pages of this volume are devoted to comprehensive indexes of names and subjects covering parts 1 and 2. The part opens with a discussion of bacillary dysentery by Dr. George Walther. Chapter 2, by Dr. Ernst Nauck, covers asiatic cholera in a systematic manner. A discussion of the different types of brucellosis in the domestic animals and man by Wilhelm Löffler and D. L. Moroni follows. This chapter contains an unusual number of illustrations: roentgenograms of the chest and osseous system, photographs of skin lesions in man, and microphotographs of the pathological lesions, some which are in color. The late Dr. Hartwig Hormann wrote the article on plague. Tularemia is discussed by Prof. Hans Schulten, tetanus by Prof. Fritz Linder, and pertussis by Prof. Eduard Reichenow. There is a general discussion of the infestations followed by articles on malaria, leishmaniasis, African sleeping sickness, Chagas' disease, Amebiasis, and on lambliasis, coccidiosis, and balantidiosis. Professor Nauck discusses bartonellosis and Professor Mohr, toxoplasmosis. Arthropods as the causes and carriers of disease are considered by Prof. Fritz Meyer and the worm diseases by Prof. H. Vogel and Dr. W. Minning. Professor Vogel covers general helminthology, nematode infestations, oxyuriasis, trichuriasis, anchylostomiasis, trichinosis, and schistosomiosis. As in the first part of volume 1, the articles are clearly written and systematically arranged; the typography and illustrations are excellent; and there are extensive bibliographies at the ends of chapters or sections. The material discussed is covered in great detail. This work compares favorably with those of similar scope in the English language.

The Musculoskeletal System: A Symposium Presented at the Twenty-Third Graduate Fortnight of the New York Academy of Medicine, October Ninth to Twentieth, 1950. Edited by Mahlon Ashford, M.D. Cloth. $6.50. Pp. 368, with 103 illustrations. The Macmillan Company, 60 Fifth Ave., New York 11, 1952.

The Graduate Fortnight of the New York Academy of Medicine has established itself, during the past 23 years, as an important undertaking in postgraduate medical education. Each year a selected topic is presented through a series of formal evening lectures, informal morning panel discussions, a large series of afternoon clinic sessions held in over 20 different hospitals, and scientific exhibits and demonstrations.

This volume contains the formal lectures on the advances in knowledge of the musculoskeletal system and its diseases. The authors, chosen for their outstanding ability, possess extensive knowledge of the subjects covered, the list of the participants including Drs. Bosworth, Bunim, Freyberg, Hatcher, Jaffe, Ragan, Snapper, and Steindler.

This collection of addresses contains some excellent material. The first two discussions are devoted to the basic structure and chemical nature of connective tissue. This is followed by a series of discussions on diseases of bones and muscles. The important physiological effects of cortisone and adrenocorticotropic hormone and pituitary-adrenal relationships are discussed. The section on the metabolism of bone is excellent. There are three lectures on arthritis and gout. The sections on tuberculosis and tumors of bones and joints are instructive, and the section on aseptic necrosis of bone is excellent. The discussions on collagen diseases, nonarticular rheumatism, and pyogenic arthritis are well written. Problems of prevention and treatment are emphasized, and the therapeutic principles essential to the understanding of each problem are stressed. Some of the discussions are highly technical.

This project will certainly enhance the education of the general practitioner. The series is up-to-date and contains many good references for further reading or research. This commendable project should be followed in every large medical center, even if it has to be underwritten or supported by private funds. This is the first volume of a series that is to appear in book form, and anyone who reads it will look forward to further similar publications.

Methods in Physical Education: An Illustrated Textbook for Students Preparing to Teach Boys and Girls in Secondary Schools. By Hilda Clute Kozman, Ph.D., Rosalind Cassidy, Ed. D., Professor of Physical Education, University of California, Los Angeles, and Chester O. Jackson, Ed. D., Professor of Physical Education, University of Illinois, Urbana. Second edition. Cloth. $5. Pp. 557, with illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, 1952.

This is a revision of an earlier edition intended primarily for the secondary school physical education teacher. Physical education is termed a medium of education for living, and emphasis is placed on instruction stressing total growth and development rather than merely a daily exercise routine for students. The procedures and point of view are closely coordinated with those of general secondary education. Teachers of physical education are regarded as educators who share with others in the educational process, although the special contributions that physical education can make are thoroughly outlined.

The first part of the book is chiefly concerned with the teachers' role and study of how secondary school youth grows and learns in an American school community. The importance of skillful guidance, careful organization, and effective presentation in the teaching process are considered in the central portions of the text. The balance of the volume is devoted to teaching aids, extraclass activities, and evaluation of the instructional program and the teachers' work.

Case studies provide a stimulating introduction for some of the chapters, and carefully developed study questions and reading lists add to the usefulness of the book. The personalized approach throughout the text should interest students and aid in relating the material to teaching problems. The volume should be of value as a reference to teachers and to students majoring in physical education.

Essentials of Public Health. By William P. Shepard, B.S., M.D., M.A. With collaboration of Charles Edward Smith, M.D., D.P.H., Rodney Rau Beard, M.D., M.P.H., and Leon Benedict Reynolds, A.B., Sc.D. With foreword by Ray Lyman Wilbur, M.D., LL.D., Sc.D., Chancellor, Stanford University, San Francisco. Second edition. Cloth. $6.50. Pp. 381, with illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; Aldine House, 10-13 Bedford St., London, W.C.2; 2083 Guy St., Montreal, 1952.

If every practicing physician had an understanding of the essentials of public health set forth in Dr. Shepard's book, the health officer's job would be a pleasant experience and our communities would be happier places in which to live. This is an elementary text for the training of medical students and for improving the understanding of public health by physicians in private practice. They admit that their objective is not to make a health officer of the clinical practitioner, and, certainly, this book would not produce a health officer, but it will give a physician sufficient understanding of how he can cooperate in his community's health protection program.

This edition has been brought up-to-date and reset in a slightly different type, which is attractive, but the headings are less easily identified than those in the first edition. A chapter on physicians and the public health nurse has been added to give the physician a better understanding of this important public health worker and help him learn how to give her the medical direction that she needs. This is a book that should be in the library of all physicians and particularly those in the smaller communities in which the physician in practice is close to his colleagues in the health department.

Infant Feeding and Feeding Difficulties. By Philip Rainsford Evans, M.D., M.Sc., F.R.C.P., Director, Department of Child Health and Children's Physician, Guy's Hospital, London, and Ronald MacKeith, M.A., D.M., M.R.C.P., Assistant Children's Physician, Guy's Hospital. Cloth. 12s.6d. Pp. 255, with 64 illustrations. J. & A. Churchill, Ltd., 104 Gloucester Place, Portman Sq., London, W.1, 1951.

This little book, written by two Guy's Hospital pediatricians, is primarily intended for students and nurses. It is written so simply and clearly that the average mother will be able to understand it. Americans will consider the section on breast feeding, which includes a chapter on the anatomy and physiology of the human breast, and the preparation of the mother for lactation as the most valuable part of the book. In fact much of the book can be considered as advice to the young physician on how to handle new mothers. Close to 100 pages are devoted to breast feeding in contrast to less than 8 pages to the theoretical discussion of the nutritional needs of infants and 15 pages to artificial feeding.

The use of trade names for artificial foods and for medicines detracts from the discussion, even though the composition of the foods is given in an appendix. One wonders why the addition of vitamins C and D to the infant's diet is delayed until the second month. The discussions of feeding problems and of nutritional disease are brief but probably adequate for their purpose. The illustrations and diagrams are clear. The quotations, usually from the classics, that head each chapter are cleverly chosen.

United States Government Organization Manual 1952-53. U. S. Federal Register Division, National Archives and Records Service, General Services Administration. Revised as of July 1, 1952. Paper. $1. Pp. 742. Superintendent of Documents, Government Printing Office, Washington 25, D. C., 1952.

All physicians today should be familiar with the activities of at least some of the departments of the federal government. Personal experience has provided some familiarity, and, yet, there are some physicians who know little about less publicized departments that may affect their lives in almost unbelievable ways. Therefore, they would be in a better position to understand modern government, its demands and its services, if they knew its organizational make-up. This manual offers such information and should be available to all physicians who pride themselves on being good citizens. It contains a wealth of material, which is presented concisely and lucidly. Young and old, student and casual reader, business man, professional man, housewife—all of these and others will find this book interesting and a handy reference.

QUERIES AND MINOR NOTES

VITAMIN DEFICIENCIES FOLLOWING USE OF ANTIBIOTICS

To the Editor:—*What happens to the vitamin elaborating intestinal bacteria when antibiotics are taken orally for a long period? I refer to such drugs as aureomycin, terramycin, and chloramphenicol (chloromycetin®).*

Lewis E. Shapiro, M.D., Hawaiian Islands.

Answer.—The effect of an antibiotic on the vitamin elaborating intestinal bacteria depends entirely on the level of the antibiotic used. Many workers have reported a beneficial effect on growth and food utilization in experimental animals fed rations containing small amounts of antibiotics. Others have found a moderating or sparing effect on the requirements for certain B complex vitamins, such as thiamine and vitamin B_6 (Antibiotics and B-Vitamin Requirements, *Nutrition Reviews* **10**:107 [April] 1952); however, in all these cases, levels of 10 to 100 mg. of antibiotic per kilogram of ration were used. This is equivalent to a daily dose of 5 to 50 mg. in human subjects. Even with these low levels, some change in intestinal flora occurs. There seems to be an increase in coliform organisms and a decrease in anaerobes. Much larger quantities of the drugs are used in clinical therapy. Gewin and Friou (Manifestations of Vitamin Deficiency During Aureomycin and Chloramphenicol Therapy of Endocarditis Due to Staphylococcus Aureus, *Yale J. Biol. & Med.* **23**:332 [Feb.] 1951) reported severe vitamin deficiency in a 22-year-old man under treatment for subacute bacterial endocarditis; in this case, therapy consisted of 3 gm. of aureomycin given daily for 13 days, followed by the same amount of aureomycin plus 3 gm. of chloramphenicol for another 20 days. (See also Vitamin Deficiency Signs During Antibiotic Therapy, *Nutrition Reviews* **9**:283 [Sept.] 1951). Doses in this range will undoubtedly produce large changes in the intestinal flora and will decrease the production of vitamins, especially B complex vitamins and vitamin K, but the additional effects of anorexia, vomiting, and diarrhea, which are common when high levels of antibiotics are used, cannot be overlooked in any consideration of vitamin deficiency.

PERIANAL IRRITATION DUE TO AUREOMYCIN

To the Editor:—*I would like information on the "side effects" of aureomycin. The side effects that usually occur are disturbances of the gastrointestinal tract resulting in diarrhea. One patient had no diarrhea but had irritation of the anus to such a degree that he considered going to bed because walking was painful. This episode occurred after a total dose of only 10 capsules of aureomycin, 250 mg. each, which cured his respiratory tract infection. Examination revealed no hemorrhoids or other lesion to account for the inflammation and pain. The condition lasted two weeks. I have seen no references in the literature to this sort of side effect.*

J. H. Stickler, M.D., Seattle.

Answer.—The intense irritation in or about the perianal tissues caused by aureomycin and terramycin is dependent on an interference with the normal flora of the colon. The resulting changes in enzyme balance seem to produce irritative phenomena in these tissues. Dr. Albert Miltzer of the Department of Microbiology of Michael Reese Hospital, Chicago, observed that if these patients are given 2 teaspoonfuls of an elixir of vitamin B_{12}, folic acid, and ferric ammonium citrate four times a day with the aureomycin or terramycin, neither the diarrhea nor the perianal irritation occur. In addition, this consultant has used suppositories consisting of 1½ grains (0.09 gm.) of sodium alkyl sulfate in coca butter as a suppository emulsion, which the patient inserts into the rectum three times a day. This consultant's experience coincides with that of the inquirer in that hemorrhoids do not account for the inflammation and pain.

Dr. Miltzer's work has not yet been published; however, it is his opinion that aureomycin and terramycin destroy the normal flora of the intestinal tract, particularly those organisms involved in the synthesis of vitamin B_{12}. Furthermore, the overgrowth of saprophytes and particularly Pseudomonas has been apparent to this consultant. The Pseudomonas organisms cause diarrhea, with loss of proteins, electrolytes, and mucus. In these patients, the use of antibiotics is stopped, the patients are put on a diet high in protein, and the flora are allowed to return to normal as soon as possible. In some patients, it has been necessary to use polymyxin B sulfate to overcome the luxurious growth of the Pseudomonas organisms. It is this consultant's opinion that combinations of either of these two antibiotics with others should rarely, if ever, be used, especially postoperatively. The electrolyte and protein balance may be disturbed, and this may increase the morbidity in any given patient. With the use of the elixir referred to, all patients who have been given either aureomycin or terramycin are, as a rule, noticeably free from gastrointestinal manifestations, including perianal irritation.

PENICILLIN AND STREPTOMYCIN

To the Editor:—*How frequently does fever occur as a side effect in treatment with penicillin? Has any deleterious effect on the myocardium from the use of streptomycin been noted?*

Bernard Drexler, M.D., Rochester, N. Y.

Answer.—Fever does not occur as a side effect in penicillin therapy unless it is associated with other signs of hypersensitivity. It is important in the use of penicillin solutions, especially when they have been prepared so that multiple doses may be given from the same container, that contamination be avoided. Occasionally, contaminated penicillin will cause fever. Deleterious effects on the myocardium from the use of streptomycin have not been noted.

PENICILLIN REACTIONS AND CHEESE

To the Editor:—*There are references in the literature to reactions to penicillin. If a patient has received penicillin before, it is understandable why he may have become sensitized, but if he has not, it is more difficult to understand. A possible explanation occurred to me. It is well known that cheese is ripened by the action of molds. I have had patients who had an allergic reaction after ingestion of one variety of cheese but who could eat another safely. Could some of the molds be closely related to Penicillium notatum and have sensitized the person who had a reaction?*

J. W. Robinson, M.D., Los Angeles.

Answer.—Some cheeses, notably Roquefort, are ripened by molds, and among these molds, members of the genus Penicillium are important. The ingestion of cheese ripened by molds would undoubtedly expose a person to the possibility of the development of an allergy to substances produced by members of this genus. It is not known, however, that this actually occurs. Another possible source of exposure is the inhalation of mold spores that are present in the atmosphere during certain seasons. There is good evidence that previous attacks of dermatophytosis may predispose to allergic reactions to penicillin of the erythematopapulovesicular type, which is most often seen on the feet and hands, but which may be generalized. At present, this seems to be the most probable source of sensitivity to penicillin in those who have not received penicillin previously.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

ERYTHROBLASTOSIS

To the Editor:—*1. Is there any substance that may be given Rh-negative patients to prevent the formation of antibodies? 2. Is there anything new that can be given these patients while they are pregnant to prevent erythroblastosis? 3. How is the Hr factor patient handled? 4. Does synkamin® (4-amino-2-methyl-1-naphthol hydrochloride) given while the patient is pregnant help to prevent this?*

Louis M. Pavletich, M.D., Raton, N. M.

Answer.—1. There is no substance that can be given to Rh-negative women to prevent formation of Rh antibodies. For sensitization to develop, it is necessary for Rh-positive blood to be introduced into the body by a parenteral route; this could occur as the result of an injection of blood or of a pregnancy with an Rh-positive fetus. Since even a fraction of 1 cc. may be sufficient to sensitize the patient, all blood that is to be injected into the body either for blood transfusion or by the intramuscular or subcutaneous route should be typed for the Rh factor, and only Rh-negative compatible blood used for Rh-negative recipients. This blood should preferably be type rh, that is, negative for all three Rh factors, Rh_0, rh′, and rh″ (*J. A. M. A.* **149:**211 [May 10] 1952), and should be further tested to exclude the presence of Rh_0 variants.

Evidence has been reported indicating that in about one-third of all pregnancies there is leakage of fetal blood into the mother's circulation antenatally, and, similarly, such leakage of blood occurs in about one-third of all deliveries (Wiener, A. S.; Nappi, R., and Gordon, E. B.: Studies in Rh Sensitization: 3. Effect of Rh-Positive Pregnancies on Rh Antibody Titer, *Blood* **6:** 789 [Sept.] 1951). Obviously, the chance for leakage to occur is greater when the implantation of the ovum is insecure, as in ectopic gestations, abortions, and placenta previa and ablatio. Theoretically, lifting heavy weights and falls or blows producing direct trauma to the uterus could also favor leakage of fetal blood into the maternal circulation, and it may be that improper diet and vitamin deficiencies affect the placental barrier adversely.

From another point of view, Wiener has suggested the injection of harmless vaccines during pregnancy. This is based on the theory of competition of antigens, whereby exposure of the body to potent antigens may reduce the likelihood of antibody production for simultaneously introduced weaker antigens; for example, if the patient is given large doses of typhoid and pertussis vaccines during the pregnancy, should fetal blood leak into her circulation her body would presumably be less likely to react to the weaker Rh antigen. Unger (Studies on Preventive and Curative Treatments of Rh Sensitization. *Am. J. Obst. and Gynec.* **58:** 1186 [Dec.] 1949) has applied this method to a large series of pregnant Rh-negative women with some measure of success; however, even if the method is effective, it has certain disadvantages. It must be applied throughout the pregnancy, since there is no way of telling when, if at all, leakage of fetal blood may occur, i. e., without correct timing the method cannot work. Secondly, only 1 in about 20 patients becomes sensitized by pregnancy; since there is no way of telling ahead of time which one is apt to become sensitized, the vaccine would have to be given to 20 patients in order to protect 1.

2. Once the patient has become sensitized to the Rh factor, the antibodies pass readily through the placenta into the fetal circulation, so that if the baby is Rh positive, erythroblastosis is virtually inevitable. By and large, the severity of the manifestations depends primarily on the antibody titer of the mother, though other factors also appear to play a role. Nothing can be given to the mother to prevent this. In selected cases excellent results have been obtained by inducing delivery when the baby is sufficiently mature, i. e., about two weeks before term, and then treating the baby at once by exchange transfusion. Antibody tests should be done periodically antenatally on all pregnant Rh-negative women. In a few cases antibodies have been absent at the beginning of the pregnancy and appeared only close to term. By inducing delivery of the mature infant immediately after the appearance of antibodies in the maternal serum, it has been possible to prevent disease in the baby. Cesarean section is never performed merely because the expectant mother is sensitized to the Rh factor; however, if there is an obstetrical indication for section, this facilitates the management of the case, because a definite time for delivery can be set. Some workers insist that premature delivery of the erythroblastotic baby is harmful. The seeming difference in opinion is probably based on confusion between the terms "prematurity" and "immaturity." By taking care that the babies are sufficiently mature before delivering them, such objections are avoided.

3. Persons who are Rh positive can be negative for one of the Hr factors; for example, persons of type Rh_1Rh_1 (20% of Caucasians) are hr′ negative; persons who are type Rh_2Rh_2 (3% of Caucasians) are hr″ negative. Such persons could become sensitized to the corresponding Hr factor, but, since the Hr factors are much less antigenic than Rh_0, such cases are rare. Therefore, when the expectant mother is Rh positive it is customary to disregard the possibility of sensitization to the Hr factor, and Hr antibody tests are ordinarily not carried out. When an Rh-positive patient has an erythroblastotic baby, the possibility of Hr sensitization, among other things, must be considered. Erythroblastosis caused by Hr sensitization is treated in the same way as that caused by Rh sensitization, except that Hr-negative blood is used instead of Rh-negative blood. If an Hr-negative woman who has already had one erythroblastotic baby becomes pregnant again, the case is managed similarly to those in which erythroblastosis is caused by Rh sensitization. Periodic Hr antibody titrations are done, and, when indicated, the baby is delivered before term and treated by exchange transfusion, using Hr-negative blood.

4. Synkamin,® a synthetic compound with physiological properties similar to those of naturally occurring vitamin K, is not known to have any salutary effect on isosensitization in pregnancy. In rare instances in which the expectant mother has a vitamin K deficiency such therapy would, of course, be indicated.

THE BASEMENT, THE THIRD FLOOR, AND THE ARTHRITIC

To the Editor:—*What are the relative humidities and barometric pressures in a building at the basement, low first floor, and third floor levels? What would be the relative effects of these on an arthritic patient? In other words, what is the optimum building level for the dwelling of these patients?*

M.D., Illinois.

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—Barometric pressures do not vary enough between the basement and the third floor to be of any significance. Humidity, however, might vary a great deal, depending on the climate, soil conditions, and type of construction. The third floor would, in general, be drier and would be preferable to the basement or ground floor for an arthritic, provided he need not climb stairs. Climbing stairs on painful knees could be more harmful than living on the ground floor.

Answer.—The difference at any one time in barometric pressures between the basement level of a building and the third floor is so small as to be of no significance as far as health is concerned. Changes in barometric pressure as they occur from day to day have been reported to influence the symptoms of the arthritic patient. Some patients feel better when the barometer falls, and others feel better when the barometer rises. The relative humidity is a ratio between the amount of water vapor actually present and that which the air could hold if saturated at any one given temperature. Thus, if the temperature falls and the total amount of water vapor in the air remains the same, the relative humidity will rise. It is impossible to state what the relative humidity may be at various levels within a given building. Relative humidity at the basement level of the building may very well be higher than the relative humidity in the upper floors, because basements tend to be cooler and the ground around them holds moisture that can enter into the air in this part of the building. Arthritic patients seem to feel better in cold dry or warm dry environments than they do in cold damp or warm damp environments. For this reason, it would probably be better from the standpoint of symptomatic improvement of arthritis if the patients did not live in basements or ground level parts of the building.

POSSIBLE PRIMARY ATONY OF THE BLADDER

To the Editor:—*A man, aged 53, had hematuria and a distended bladder. A suprapubic exploration was done and nothing was found, except for a huge, distended, atonic bladder. Suprapubic drainage was done for six days, and the fistula closed spontaneously. The atonicity has again become evident. The patient voids at least five times in 24 hours for a total of about 80 oz. (2.4 liters) of urine. He is catheterized every three days, and a residual urine of between 70 and 80 oz. (2.1 and 2.4 liters) is obtained. There is no obvious obstruction, a no. 18 soft rubber French catheter being passed without difficulty. There is a questionable possibility that he had urethral strictures several years ago. A daughter has congenital dilatation of the colon (Hirschsprung's disease). A neurological consultant noted no abnormalities on examination. The spinal fluid is normal. The patient has been taking bethanechol (urecholine®) chloride, 2 tablets three times daily, for three weeks, without effect. Two methods of treatment have been proposed, a transurethral resection and presacral neurectomy. May I have your opinion?* *M.D., Massachusetts.*

Answer.—One cannot be sure from the information given that bladder neck or urethral obstruction is not the cause of the residual urine. The fact that a no. 18 French catheter will pass readily into the bladder is not evidence of lack of mechanical obstruction in the urethra or bladder neck. The differential diagnosis lies among mechanical obstruction, an obscure neurogenic lesion causing spinal pressure, and primary atony of the bladder. A few patients such as the one described have been seen by this consultant, in whom either a diverticulum of the bladder came forward under the prostatic urethra to cause residual urine, or a utricular cyst was present and pressed up on the bladder neck from below. Before doing either a transurethral resection or presacral neurectomy, this patient should be studied most carefully. Cystograms and urethrograms should be made, and a careful urethroscopic study of the prostatic portion of the urethra and bladder neck should be made with a fore oblique telescope. It is unscientific to treat a patient of this sort with bethanechol when a definite diagnosis has not been made. A presacral neurectomy would not seem indicated, even if it could be proved that this is a case of primary atony of the bladder. This latter condition is rare and is usually the aftermath of a prolonged overdistention from a temporary condition, following such procedures as spinal anesthesia, operative procedures on the rectum and anus, or repair of an inguinal hernia. It would seem that this is a case of vesicle neck obstruction with secondary atony of the bladder, in which case a transurethral resection and rather prolonged urethral catheter drainage of the bladder would be indicated.

SHREDS IN URINE

To the Editor:—*I would like information on the treatment of shreds that appear in the first glass of urine. I refer to shreds that can be seen in the urine with the naked eye but that reveal under the microscope strands encased with numerous pus cells. Please discuss treatment of shreds that persist following a case of gonorrhea and also those shreds that occur in the absence of a history of gonorrhea.* *M.D., Iowa.*

Answer.—Shreds that appear in the first glass of urine are indicative of some irritative lesion anterior to the triangular ligament or the so-called external sphincter. They are commonly seen in chronic urethritis and urethral stricture, either posttraumatic or postgonorrheal. If the shreds are examined under the microscope they are seen to contain mucus, polymorphonuclear leukocytes, and a small number of bacteria. If infection of the upper urinary tract has been ruled out by cultures of the second voided specimen of urine, the urethra should be calibrated by the passage of bulbous bougies (bougie à boule). If stricture is shown to be present, the urethra should be dilated with metal sounds once weekly, the sounds being enlarged by ⅓ mm. at each treatment (1F). Following the dilatation of the urethra, colloidal solutions of mild silver protein (5% silvol® or argyrol®), or, later, weak solutions of silver nitrate, ⅛ to ¼%, should be injected. Recently, 0.05% tyrothricin has been used with success.

RADIOACTIVE IODINE AND THYROTOXICOSIS

To the Editor:—*A 30-year-old man has had persistent tachycardia and palpitations, apparently of toxic origin. The basal metabolic rate is +25 and the blood cholesterol level 137 mg. per 100 cc. Therapy with a saturated solution of potassium iodide, 10 drops twice daily, has resulted in a remission of symptoms and a decrease in the heart rate. Would it be advisable to try to obtain a permanent remission with the use of radioactive iodine?*

J. S. Lane, M.D., Lexington Park, Md.

Answer.—Opinions differ among investigators using radioactive iodine in thyrotoxicosis concerning the criteria for selection of patients for this type of therapy. More than a decade has elapsed since radioactive iodine was first administered to a human. There has been, as yet, no report of adverse radiation effects in any of the patients who have received radioactive iodine for the treatment of hyperthyroidism, but the majority of investigators still believe that in young persons with uncomplicated thyrotoxicosis, surgical intervention is probably the treatment of choice. This young man's trouble would appear to be due to hyperthyroidism, since he had such an excellent remission following the administration of potassium iodide. He would certainly obtain an excellent result from a therapeutic dose of radioactive iodine. If this therapy were decided on, administration of potassium iodide would have to be discontinued for a period of from three to four weeks before administration of radioactive iodine. Unless this young man absolutely refuses surgical treatment or has some concurrent disease that contraindicates surgery, it is the treatment of choice after proper preparation.

MILIARY TUBERCULOSIS

To the Editor:—*I have been treating a patient with miliary tuberculosis for almost six months. She has been receiving streptomycin and paraaminosalicylic acid and clinically has shown excellent improvement. Roentgenograms of the chest reveal very little change, however. She is frequently afebrile, and the sputum is negative on direct smear. Would it be advisable to start this patient on isoniazid (isonicotinic acid hydrazid) because of the generally poor prognosis of such a case, or would it be better to reserve this new drug for future use if indications of retrogression appear?*

Floyd H. Brigham, M.D., Rusk, Texas.

Answer.—Since this patient has done so well on the streptomycin and paraaminosalicylic acid treatment and since bacterial resistance is slow to develop on that combination and no severe damage to the labyrinth has been reported, it would seem best to continue this treatment for several more months. Isoniazid can be held in reserve and used if the others begin to fail. In the interim, it may be learned more definitely what is the best dosage of isoniazid in such cases and especially whether there is any advantage in combining it with streptomycin, paraaminosalicylic acid, or other drugs. At this time there does seem to be much to be gained in combining isoniazid with streptomycin, but it is still too soon to make a recommendation of the use of such a combination. If the combination does as much as that of streptomycin and paraaminosalicylic acid to keep down resistance of the tubercle bacilli, it will be worthwhile.

MEASLES

To the Editor:—*Is there any contraindication to exposing a healthy child to a patient with measles, if the child has received gamma globulin? How many minutes would be considered sufficient for exposure?* *M.D., New York.*

Answer.—Even though the administration of gamma globulin before exposure to measles will modify an attack of the disease, planned exposure is not advisable. Very rarely, serious complications develop with "mild measles." The length of time required for infection would depend primarily on two conditions: (*a*) the stage of measles in the patient and (*b*) the proximity of exposure. Measles is most contagious just before and immediately after appearance of the eruption. A susceptible person could be infected within 10 seconds.

INTERCOSTAL NEURALGIA FOLLOWING SYMPATHECTOMY

To the Editor:—*Malignant hypertension, which did not respond to conservative measures, developed in a 42-year-old housewife. The blood pressure has been about 240/150 mm. Hg during the last two months. A sympathectomy of the dorsolumbar type was performed. Careful study prior to operation failed to show evidence of kidney damage or cardiac enlargement or other persistent effects other than a retinal hemorrhage. The patient accepted the sympathectomy because of persistent headaches which totally disabled her and were accompanied by a radiating facial neuralgia similar to* tic douloureux. *Following the second stage of the sympathectomy, severe radiating girdle pain around the region of the last two ribs on either side developed. This pain was sometimes described as a burning sensation and at other times as a throbbing feeling; at times she feels as though the ribs are coming through the skin. This obviously relates in some way to the resection of a portion of the last two ribs and the interruption of the sympathetic pathways. Her blood pressure since operation has been 130/90 to 149/90 mm. Hg. The headaches and neuralgia of the face have disappeared. It is now six months since the sympathectomy was done, and for the last three months the back pain and neuralgia have never been completely relieved. Methadone hydrochloride in 5 mg. doses was used at night so the patient could get some sleep. She cannot stand to have the lightest clothing touch her back, because it causes severer pain. What treatment is suggested for this type of neuralgia? How long will it continue?*

M.D., Arizona.

Answer.—The intercostal neuralgia following resection of ribs during the course of dorsolumbar sympathectomy usually disappears in six to eight weeks, although its severity and duration varies a great deal. While this neuralgia is a well-known complication of transthoracic operations requiring rib resection, undoubtedly, the sympathectomy itself contributes to this painful complication, since it is observed after lumbar sympathectomies involving no removal of ribs; it also seems to occur more frequently and with more severity in the advanced, premalignant, or malignant forms of hypertension. Traction on nerve trunks by retractors or ribspreaders, perineural fibrosis, and ischemia of posterior root ganglion as a result of interruption of the slender little branch which nourishes it, are possible causes of severe, long lasting neuralgia. This may last for months, but it decreases in severity and seldom lasts longer than a year. The injection of massive doses of vitamin B_{12} (from 300 to 500 μg. daily) offers the most promise of relief; the earlier it is used after the onset of pain, the more definite the relief that may be expected.

ONE OVARY AND CHANCES FOR PROCREATION

To the Editor:—*What are the chances for procreation in a 20-year-old- woman who has had an ovary removed and has irregular and abundant menstruation?*

Henri Rathle, M.D., Brooklyn.

Answer.—The removal of one ovary should not per se lessen a woman's chances for procreation. Whether irregular and abundant menstruation can be a factor in doing so would depend on the cause of such a menstrual abnormality, although it is probably functional; for example, if the woman has a functional anovulatory hypermenorrhea, the prospects are good for the later reestablishment of a normal menstrual mechanism. If this girl is married and if her present problem is that of sterility, a far more intelligent prognosis could be given if the customary sterility studies of both wife and husband are done than is possible from the incomplete data given in the query.

CUTTING THE FRENULUM

To the Editor:—*Do you believe that cutting the frenulum is ever justified to correct some speech defect or nursing difficulty?* *Karl J. Deissler, M.D., Oakland, Calif.*

Answer.—The frenulum of the tongue is a vertical fold of mucous membrane under the tongue. Operative interference by dividing the frenum close to the undersurface of the tongue is seldom required. Newborn infants, particularly, are thought to be tongue-tied when the frenum actually is of normal length. Rarely, there is a shortening of the frenum that makes it impossible for the infant or child to protrude the tongue to a normal extent, thus interfering with articulation and even with sucking. In general, it may be stated that if the tongue can be protruded beyond the lips, no treatment is necessary. Further, it should be realized that indiscriminate cutting of the frenum linguae may result in severing of the lingual artery and serious hemorrhage. Occasionally, if speech is impaired, it may be necessary to snip the frenum of the lower lip and gum.

INFECTIOUS HEPATITIS AND PREGNANCY

To the Editor:—*The answer to a query in* The Journal *July 19, 1952, page 1174, on whether infectious hepatitis contracted during pregnancy should be considered a cause for therapeutic abortion stated, "there are apparently no reports of the disease affecting the offspring in utero." Dr. J. E. Wesp and I reported a case* (Am. J. Obst. & Gynec. **62**:*1153-1156 [Nov.] 1951) in which the mother was affected with infectious hepatitis during the first trimester of pregnancy and the infant was a composite monster. A review of the literature revealed no other case in which the infant was affected; however, there was no other case in which the disease was contracted by the mother during the first trimester of pregnancy. Apparently it is during this early period of gestation that as is the case with rubella, the damage is done to the fetus.*

C. S. Kellogg, M.D.
98 Cherry St., Swanton, Ohio

PEDICULOSIS OF EYELASHES

To the Editor:—*I would like to comment on the Query and Minor Note "Pediculosis of Eyelashes" in* The Journal *June 21, 1952, page 797. One per cent yellow oxide of mercury ointment will not eradicate pediculosis pubis from the eyelashes. If your consultant had ever had pediculosis he would know that mild mercurial ointment should be applied to the lashes with a small cotton swab. An adult should attend the child for 30 minutes to keep him from rubbing the eyes. The ointment should then be removed with dry cotton or gauze. The small amount left will do no harm. The treatment should be repeated the next day or two days later. If done properly, these two treatments will kill the lice and destroy their eggs. The source of the infestation, of course, should be treated with the same medicament.* *J. J. Horton, M.D.*
Buda, Texas.

MILD CONVULSIVE SEIZURES IN INFANT

To the Editor:—*In reference to a query in* The Journal *July 12, 1952, page 1263, on convulsive seizures in an infant I would like to suggest that an intracranial pathological condition should be considered as a possible cause, in addition to those mentioned in the reply. Various congenital defects of the brain, hemorrhages (old), and tumors can occur intracranially in infants, although they are rare. A thorough neurological study, including encephalographic examination and examination of the eye grounds, should be undertaken. I had a similar case in which the cause turned out to be a cerebral defect. Subdural taps at the lateral angles of the anterior fontanelle in infants help to determine the presence of subdural hematomas.*

Jacob Greenblatt, M.D.
1675 Bedford St.
Stamford, Conn.

NIGHT CRAMPS IN LEGS

To the Editor:—*In the query "Night Cramps in Legs" in* The Journal *July 5, 1952 (page 978), the consultant suggests quinine sulfate and diphenhydramine hydrochloride as prophylactics for this painful condition. For relief of attacks, I have found sublingually administered glycerol trinitrate wonderfully effective. The relief is immediate and complete. The mechanism is probably the same as occurs in relief of angina pectoris.* *W. H. Powe, M.D.*
202 Brown St., Greenville, S. C.